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L18	L16 and cre	15	L18
L17	L16 and L15	6	L17
L16	codon near3 mammal$	238	L16
L15	cre recombinase	528	L15
L14	modif$ near3 cre recombinase	1	L14
L13	L11 and cre	0	L13
L12	L11 and L10	0	L12
L11	(L9 and cre) AnD ((@pd > 20020509!))	0	L11
L10	(L9 and L8) AnD ((@pd > 20020509!))	0	L10
L9	cre recombinase	528	L9
L8	(cre recombinase) AnD ((@pd > 20020509!))	0	L8
L7	(modif$ near3 cre recombinase) AnD ((@pd > 20020509!))	0	L7
L6	L4 and cre	15	L6
L5	L4 and l2	6	L5
L4	codon near3 mammal$	238	L4
L3	codone near3 mammal$	0	L3
L2	cre recombinase	528	L2
L1	modif$ near3 cre recombinase	1	L1

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NEWS 4 Feb 01 DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS 5 Feb 19 Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 6 Mar 08 Gene Names now available in BIOSIS
NEWS 7 Mar 22 TOXLIT no longer available
NEWS 8 Mar 22 TRCTHERMO no longer available
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L1 870 WHOLE BODY IMAG?

=> s l1 and fluor?
L2 109 L1 AND FLUOR?

=> s l1 and (GFP or EGFP or BFP or RFP)
L3 13 L1 AND (GFP OR EGFP OR BFP OR RFP)

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 7 DUP REM L3 (6 DUPLICATES REMOVED)

=> d bib abs 1-

YOU HAVE REQUESTED DATA FROM 7 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 2002:241581 BIOSIS
DN PREV200200241581
TI Real-time optical imaging of primary tumor growth and multiple metastatic events in a pancreatic cancer orthotopic model.
AU Bouvet, Michael; Wang, Jinwei; Nardin, Stephanie R.; Nassirpour, Rounak; Yang, Meng; Baranov, Eugene; Jiang, Ping; Moossa, A. R.; Hoffman, Robert M. (1)
CS (1) AntiCancer, Inc., San Diego, CA, 92111: all@anticancer.com USA
SO Cancer Research, (March 1, 2002) Vol. 62, No. 5, pp. 1534-1540. http://cancerres.aacrjournals.org/. print. ISSN: 0008-5472.
DT Article
LA English
AB We report here whole-body optical imaging, in real time, of genetically fluorescent pancreatic tumors growing and metastasizing to multiple sites in live mice. The whole-body optical imaging system is external and noninvasive. Human pancreatic tumor cell lines, BxPC-3 and MiaPaCa-2, were engineered to stably express high-levels of the Aequorea victoria green fluorescent protein (***GFP***). The ***GFP*** -expressing pancreatic tumor cell lines were surgically orthotopically implanted as tissue fragments in the body of the pancreas of nude mice. Whole-body optical images visualized real-time primary tumor growth and formation of metastatic lesions that developed in the spleen, bowel, portal lymph nodes, omentum, and liver. Intravital images in the opened animal confirmed the identity of ***whole*** - ***body*** ***images*** . The ***whole*** - ***body*** ***images*** were used for real-time, quantitative measurement of tumor growth in each of these organs. Intravital imaging was used for quantification of growth of micrometastasis on the liver and stomach. ***Whole*** - ***body*** ***imaging*** was carried out with either a trans-illuminated epi-fluorescence microscope or a fluorescence light box, both with a thermoelectrically cooled color CCD camera. The simple, noninvasive, and highly selective imaging made possible by the strong ***GFP*** fluorescence allowed detailed simultaneous quantitative imaging of tumor growth and multiple metastasis formation of pancreatic cancer. The ***GFP*** imaging affords unprecedented continuous visual monitoring of malignant growth and spread within intact animals without the need for anesthesia, substrate injection, contrast agents, or restraint of animals required by other imaging methods. The ***GFP*** imaging technology presented in this report will facilitate studies of modulators of pancreatic cancer growth, including inhibition by potential chemotherapeutic agents.

L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2002 ACS
AN 2001:713588 CAPLUS
DN 135:254092
TI Whole-body optical imaging of gene expression and its use in drug screening and evaluation of therapeutic protocols
IN Yang, Meng; Baranov, Eugene
PA Anticancer, Inc., USA
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001071009	A2	20010927	WO 2001-US8947	20010319
W: AU, CA, JP, KR				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
US 2002013954	A1	20020131	US 2001-812710	20010319

PRAI US 2000-190196P P 20000317
AB The invention relates to the whole-body external optical imaging of gene expression. Specifically, methods for whole-body external optical imaging of gene expression and methods for evaluating a candidate protocol or drug for treating diseases or disorders using a fluorophore operatively linked to the promoter of a gene and external optical imaging are provided herein. Methods to screen for substances or genes that regulate target promoters are also provided. The method uses a gene for a fluorescent reporter protein under the control of a tissue- or disease-specific promoter. Gene expression can be monitored either in live animals using transillumination or after dissection. Delivery of green fluorescent protein genes into mice for whole body monitoring is demonstrated.

L4 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 2001:430979 BIOSIS
DN PREV200100430979
TI Spatial-temporal imaging of bacterial infection and antibiotic response in intact animals.
AU Zhao, Ming; Yang, Meng; Baranov, Eugene; Wang, Xiaoen; Penman, Sheldon; Moossa, A. R.; Hoffman, Robert M. (1)
CS (1) AntiCancer, Inc., 7917 Ostrow Street, San Diego, CA, 92111: all@anticancer.com USA
SO Proceedings of the National Academy of Sciences of the United States of America, (August 14, 2001) Vol. 98, No. 17, pp. 9814-9818. print. ISSN: 0027-8424.

DT Article
LA English
SL English
AB We describe imaging the luminance of green fluorescent protein (***GFP***)-expressing bacteria from outside intact infected animals. This simple, nonintrusive technique can show in great detail the spatial-temporal behavior of the infectious process. The bacteria, expressing the ***GFP*** , are sufficiently bright as to be clearly visible from outside the infected animal and recorded with simple equipment. Introduced bacteria were observed in several mouse organs including the peritoneal cavity, stomach, small intestine, and colon. Instantaneous real-time images of the infectious process were acquired by using a color charge-coupled device video camera by simply illuminating mice at 490 nm. Most techniques for imaging the interior of intact animals may require the administration of exogenous substrates, anesthesia, or contrasting substances and require very long data collection times. In contrast, the whole-body fluorescence imaging described here is fast and requires no extraneous agents. The progress of Escherichia coli- ***GFP*** through the mouse gastrointestinal tract after gavage was followed in real-time by ***whole*** - ***body*** ***imaging*** . Bacteria, seen first in the stomach, migrated into the small intestine and subsequently into the colon, an observation confirmed by intravital direct imaging. An i.p. infection was established by i.p. injection of E. coli- ***GFP*** . The development of infection over 6 h and its regression after kanamycin treatment were visualized by ***whole*** - ***body*** ***imaging*** . This imaging technology affords a powerful approach to visualizing the infection process, determining the tissue specificity of infection, and the spatial migration of the infectious agents.

L4 ANSWER 4 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:152084 BIOSIS
DN PREV200200152084
TI Myc-driven lymphomas respond with both apoptosis and senescence to anticancer treatment in vivo.
AU Schmitt, Clemens A. (1); Yang, Meng; Fridman, Jordan S.; Baranov, Euguge; Hoffman, Robert M.; Lowe, Scott W.
CS (1) Max-Delbruck-Center for Molecular Medicine, Hematology/Oncology, Charite, Humboldt-University, Campus Virchow Hospital, Berlin Germany
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 2, pp. 172b. http://www.bloodjournal.org/. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 2 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971.
DT Conference
LA English
AB Apoptosis and premature senescence are fundamental tumor suppressor programs against oncogene-mediated transformation. For example, oncogenic ras has been implicated in p16-mediated senescence while the c-myc oncogene promotes cell death, mainly in a p53-dependent manner. In turn, either program can become a mutational target depending on the driving oncogene. In fact, mutations of p53 or the INK4a/ARF locus, encoding p16 and the p53 regulator ARF, are common events in most tumor entities. Moreover, since many anticancer agents induce apoptosis, apoptotic defects may contribute to chemoresistance. Using the Emu-myc transgenic mouse lymphoma model, we examined to what extent genetic defects in the INK4a/ARF and p53 loci impair drug-induced long-term cell cycle arrest and apoptosis in myc-driven B-cell lymphomas in vivo. Myc-transgenic mice with heterozygous targeted disruption of either the ARF, the INK4a/ARF or the p53 locus rapidly develop lymphomas which are typically null for the respective loci due to loss of heterozygosity (LOH). Consequently, these tumors display apoptotic defects. Competitive introduction of the anti-apoptotic bcl-2 gene into ARF+/-, INK4a/ARF+/- or p53+/- myc-transgenic hematopoietic stem cells is sufficient to establish lymphomas without LOH. However, when treated with cyclophosphamide in vivo, ARF null lymphomas do not reproduce the poor response observed in INK4a/ARF null or p53 null lymphomas, but are prone to a reciprocal LOH of the retained INK4a allele (which encodes p16). While INK4a/ARF null or p53 null lymphomas progress quickly to a terminal stage upon treatment failure, control lymphomas (i.e. myc-driven lymphomas without a targeted lesion) engineered to harbor solely a Bcl-2 mediated apoptotic defect fail to achieve remissions, but remain stable over weeks as assessed by clinical observation and ***whole*** ***body*** ***imaging*** of living animals bearing ***GFP*** -tagged lymphomas. Proliferation markers indicate that those lymphomas respond to cyclophosphamide with a long-term cell cycle arrest. This arrest is associated with prolonged upregulation of both p53 and p16 protein levels. However, only control lymphomas turn positive for the senescence associated beta-galactosidase (SA-beta-Gal) activity within days after treatment, while p53 null lymphomas - despite high p16 protein levels - fail to arrest and to display SA-beta-Gal activity in situ. Therefore, p16 controls a p53-mediated senescence-like arrest program in myc-driven lymphomas upon DNA damaging treatment in vivo. These findings provide important insights into the genetic links between tumorigenesis and chemoresistance: ARF mutations disabling Myc signaling to p53, for example, disrupt a central tumor suppressor mechanism, but unlike mutations in p53, which controls both apoptosis and arrest, cannot co-select for resistance to drug-induced senescence.

L4 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
AN 2001:12806 BIOSIS
DN PREV200100012806
TI Visualizing gene expression by whole-body fluorescence imaging.
AU Yang, Meng; Baranov, Eugene; Moossa, A. R.; Penman, Sheldon; Hoffman, Robert M. (1)
CS (1) AntiCancer, Inc., 7917 Ostrow Street, San Diego, CA, 92111: all@anticancer.com USA
SO Proceedings of the National Academy of Sciences of the United States of America, (October 24, 2000) Vol. 97, No. 22, pp. 12278-12282. print.
ISSN: 0027-8424.
DT Article
LA English
SL English
AB Transgene expression in intact animals now can be visualized by noninvasive techniques. However, the instruments and protocols developed so far have been formidable and expensive. We describe here a system for rapidly visualizing transgene expression in major organs of intact live mice that is simple, rapid, and eminently affordable. Green fluorescent protein (***GFP***) is expressed in the cells of brain, liver, pancreas, prostate, and bone, and its fluorescence is encoded in whole-body optical images. For low-magnification images, animals are illuminated atop a fluorescence light box and directly viewed with a thermoelectrically cooled color charge-coupled device camera. Higher-magnification images are made with the camera focused through an epi-fluorescence dissecting microscope. Both nude and normal mice were labeled by directly injecting 8 X 1010 plaque-forming units/ml of adenoviral ***GFP*** in 20-100 mul PBS and 10% glycerol into either the brain, liver, pancreas, prostate, or bone marrow. Within 5-8 h after adenoviral ***GFP*** injection, the fluorescence of the expressed ***GFP*** in brain and liver became visible, and ***whole*** - ***body*** ***images*** were recorded at video rates. The ***GFP*** fluorescence continued to increase for at least 12 h and remained detectable in liver for up to 4 months. The system's rapidity of image acquisition makes it capable of real-time recording. It requires neither exogenous contrast agents, radioactive substrates, nor long processing times. The method requires only that the expressed gene or promoter be fused or operatively linked to ***GFP*** . A comparatively modest investment allows the study of the therapeutic and diagnostic potential of suitably tagged genes in relatively opaque organisms.

L4 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:300206 BIOSIS
DN PREV200100300206
TI Visualizing leukemia & lymphoma cell homing and quantification of tumor burden in response to therapy in living animals.
AU Edinger, Matthias (1); Verneris, Michael R. (1); Cao, Yuan (1); Bachmann, Michael H. (1); Costa, Gina L. (1); Contag, Christopher H. (1); Negrin, Robert S. (1)
CS (1) Departments of Medicine and Pediatrics, Stanford University, School of Medicine, Stanford, CA USA
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 123a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DT Conference
LA English
SL English
AB Revealing the mechanisms of neoplastic disease and enhancing our ability to intervene in these processes requires an increased understanding of cellular and molecular changes as they occur in living animals. We have previously shown, that since light is transmitted through mammalian tissues at a low level, we can detect light emission from tumor cells that express luciferase from within living animals, using low light imaging cameras. To establish animal models of leukemia and lymphoma, we used the A20 and Bcl1 lymphoma cell lines. A20 cells were transfected with the pCDNA3.1-luc plasmid containing a modified luciferase gene (A20-luc). Using light emission as an indicator, tumor engraftment, exponential growth and rejection was followed in individual animals after sc, iv and ip injections. Tumor engraftment in spleen, liver and lymph nodes could be localized. As few as 103 A20-luc cells could be detected after sc injection. Following iv injection of 104 A20-luc cells in a syngeneic BMT model, leukemic disease was observed with tumor infiltration of the femurs, humeri, sternum, vertebrae and skull. A retroviral transduction system was used to transfer the gene for a ***GFP*** /luc fusion protein to the Bcl1 lymphoma, known to localize to liver and spleen. ***GFP*** expressing cells were sorted by FACS and injected into mice iv. Initially, as few as 7000 tumor cells could be detected, and subsequently tumor engraftment in liver and spleen was observed. Tumor growth was followed over time and quantified from these internal organs. We also investigated the therapeutic application of cytotoxic cells termed cytokine induced killer cells (CIK) which co-express T cell and NK cell markers and are generated by in vitro expansion from splenocytes. Treatment of A20-luc tumor bearing animals with 107 CIK cells led to a decrease of tumor signal from sc growing tumors and 75% of the mice were cured within 2 wks. To examine trafficking of these activated T cells we used the retroviral transduction method to label the cells. After iv injection transduced cells were detected in the lungs, 12 h later they locate to liver and spleen, and generalize thereafter. We conclude, that ***whole*** ***body*** ***imaging*** of labeled tumor cells reveals patterns of systemic disease allowing visualization of minimal disease and therapeutic response. This will improve our insights in tumor biology, be useful in directing subsequent ex vivo assays, and provide a powerful tool to examine the kinetics of response to novel therapies.

L4 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:502217 BIOSIS
DN PREV200000487795
TI ***GFP*** tumor, metastasis and angiogenesis ***whole*** - ***body*** ***imaging*** .
AU Yang, M. (1); Baranov, E. (1); Jiang, P. (1); Sun, F.-X. (1); Li, L. (1); Hasegawa, S.; Al-Tuwaijri, M.; Shimada, H.; Moossa, A. R.; Hoffman, R. (1)
CS (1) AntiCancer, Inc., San Diego, CA, 92111 USA
SO Clinical & Experimental Metastasis, (1999) Vol. 17, No. 9, pp. 747. print.
Meeting Info.: VIII International Congress of the Metastasis Research Society London, UK September 24-27, 2000
ISSN: 0262-0898.
DT Conference
LA English
SL English

=> d his

(FILE 'HOME' ENTERED AT 18:58:33 ON 08 MAY 2002)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 18:58:42 ON 08 MAY 2002
L1 870 S WHOLE BODY IMAG?
L2 109 S L1 AND FLUOR?
L3 13 S L1 AND (GFP OR EGFP OR BFP OR RFP)
L4 7 DUP REM L3 (6 DUPLICATES REMOVED)

=> s whole body (3a)imag?
L5 1836 WHOLE BODY (3A) IMAG?

=> s l5 and (GFP or EGFP or BFP or RFP)
L6 19 L5 AND (GFP OR EGFP OR BFP OR RFP)

=> s dup rem l6
MISSING OPERATOR REM L6
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=> dup rem l6
PROCESSING COMPLETED FOR L6
L7 10 DUP REM L6 (9 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 10 ANSWERS - CONTINUE? Y/(N):y

L7 ANSWER 1 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
1
AN 2002:241581 BIOSIS
DN PREV200200241581
TI Real-time optical imaging of primary tumor growth and multiple metastatic events in a pancreatic cancer orthotopic model.
AU Bouvet, Michael; Wang, Jinwei; Nardin, Stephanie R.; Nassirpour, Rounak; Yang, Meng; Baranov, Eugene; Jiang, Ping; Moossa, A. R.; Hoffman, Robert M. (1)
CS (1) AntiCancer, Inc., San Diego, CA, 92111: all@anticancer.com USA
SO Cancer Research, (March 1, 2002) Vol. 62, No. 5, pp. 1534-1540.
http://cancerres.aacrjournals.org/. print.
ISSN: 0008-5472.
DT Article
LA English
AB We report here ***whole*** - ***body*** optical ***imaging*** , in real time, of genetically fluorescent pancreatic tumors growing and metastasizing to multiple sites in live mice. The ***whole*** - ***body*** optical ***imaging*** system is external and noninvasive. Human pancreatic tumor cell lines, BxPC-3 and MiaPaCa-2, were engineered to stably express high-levels of the Aequorea victoria green fluorescent protein (***GFP***). The ***GFP*** -expressing pancreatic tumor cell lines were surgically orthotopically implanted as tissue fragments in the body of the pancreas of nude mice. ***Whole*** - ***body*** optical ***images*** visualized real-time primary tumor growth and formation of metastatic lesions that developed in the spleen, bowel, portal lymph nodes, omentum, and liver. Intravital images in the opened animal confirmed the identity of ***whole*** - ***body*** ***images*** . The ***whole*** - ***body*** ***images*** were used for real-time, quantitative measurement of tumor growth in each of these organs. Intravital imaging was used for quantification of growth of micrometastasis on the liver and stomach. ***Whole*** - ***body*** ***imaging*** was carried out with either a trans-illuminated epi-fluorescence microscope or a fluorescence light box, both with a thermoelectrically cooled color CCD camera. The simple, noninvasive, and highly selective imaging made possible by the strong ***GFP*** fluorescence allowed detailed simultaneous quantitative imaging of tumor growth and multiple metastasis formation of pancreatic cancer. The ***GFP*** imaging affords unprecedented continuous visual monitoring of malignant growth and spread within intact animals without the need for anesthesia, substrate injection, contrast agents, or restraint of animals required by other imaging methods. The ***GFP*** imaging technology presented in this report will facilitate studies of modulators of pancreatic cancer growth, including inhibition by potential chemotherapeutic agents.

L7 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2002 ACS
AN 2001:713588 CAPLUS
DN 135:254092
TI ***Whole*** - ***body*** optical ***imaging*** of gene expression and its use in drug screening and evaluation of therapeutic protocols
IN Yang, Meng; Baranov, Eugene
PA Anticancer, Inc., USA
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001071009	A2	20010927	WO 2001-US8947	20010319
W: AU, CA, JP, KR				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
US 2002013954	A1	20020131	US 2001-812710	20010319

PRAI US 2000-190196P P 20000317
AB The invention relates to the ***whole*** - ***body*** external optical ***imaging*** of gene expression. Specifically, methods for ***whole*** - ***body*** external optical ***imaging*** of gene expression and methods for evaluating a candidate protocol or drug for treating diseases or disorders using a fluorophore operatively linked to the promoter of a gene and external optical imaging are provided herein. Methods to screen for substances or genes that regulate target promoters are also provided. The method uses a gene for a fluorescent reporter protein under the control of a tissue- or disease-specific promoter. Gene expression can be monitored either in live animals using transillumination or after dissection. Delivery of green fluorescent protein genes into mice for whole body monitoring is demonstrated.

L7 ANSWER 3 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
2
AN 2001:430979 BIOSIS
DN PREV200100430979
TI Spatial-temporal imaging of bacterial infection and antibiotic response in intact animals.
AU Zhao, Ming; Yang, Meng; Baranov, Eugene; Wang, Xiaoen; Penman, Sheldon;
Moossa, A. R.; Hoffman, Robert M. (1)
CS (1) AntiCancer, Inc., 7917 Ostrow Street, San Diego, CA, 92111: all@anticancer.com USA
SO Proceedings of the National Academy of Sciences of the United States of America, (August 14, 2001) Vol. 98, No. 17, pp. 9814-9818. print.
ISSN: 0027-8424.
DT Article
LA English
SL English
AB We describe imaging the luminance of green fluorescent protein (***GFP***)-expressing bacteria from outside intact infected animals. This simple, nonintrusive technique can show in great detail the spatial-temporal behavior of the infectious process. The bacteria, expressing the ***GFP*** , are sufficiently bright as to be clearly visible from outside the infected animal and recorded with simple equipment. Introduced bacteria were observed in several mouse organs including the peritoneal cavity, stomach, small intestine, and colon. Instantaneous real-time images of the infectious process were acquired by using a color charge-coupled device video camera by simply illuminating mice at 490 nm. Most techniques for imaging the interior of intact animals may require the administration of exogenous substrates, anesthesia, or contrasting substances and require very long data collection times. In contrast, the ***whole*** - ***body*** fluorescence ***imaging*** described here is fast and requires no extraneous agents. The progress of Escherichia coli- ***GFP*** through the mouse gastrointestinal tract after gavage was followed in real-time by ***whole*** - ***body*** ***imaging*** . Bacteria, seen first in the stomach, migrated into the small intestine and subsequently into the colon, an observation confirmed by intravital direct imaging. An i.p. infection was established by i.p. injection of E. coli- ***GFP*** . The development of infection over 6 h and its regression after kanamycin treatment were visualized by ***whole*** - ***body*** ***imaging*** . This ***imaging*** technology affords a powerful approach to visualizing the infection process, determining the tissue specificity of infection, and the spatial migration of the infectious agents.

L7 ANSWER 4 OF 10 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 3
AN 2001175177 EMBASE
TI Visualization of ***GFP*** -expressing tumors and metastasis in vivo.
AU Hoffman R.M.
CS Dr. R.M. Hoffman, AntiCancer, Inc., 7917 Ostrow Street, San Diego, CA 92111, United States. all@anticancer.com
SO BioTechniques, (2001) 30/5 (1016-1026).
Refs: 45
ISSN: 0736-6205 CODEN: BTNQDO
CY United States
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy

016 Cancer
029 Clinical Biochemistry
037 Drug Literature Index
LA English
SL English
AB We have developed mouse models of metastatic cancer with genetically fluorescent tumors that can be imaged in fresh tissue, in situ, as well as externally. To achieve this capability, we have transduced the green fluorescent protein (***GFP***) gene, cloned from the bioluminescent jellyfish Aequorea victoria, into a series of human and rodent cancer cell lines that were selected in vitro to stably express ***GFP*** in vivo after transplantation to metastatic rodent models. Techniques were also developed for transduction of tumors by ***GFP*** in vivo. With this fluorescent tool, we detected and visualized for the first time tumors and metastasis in fresh viable tissue or in situ in host organs down to the single-cell level. ***GFP*** tumors on the colon, prostate, breast, brain, liver, lymph nodes, lung, pancreas, bone, and other organs can also be visualized externally, transcutaneously by quantitative ***whole*** - ***body*** fluorescence optical ***imaging*** . Real-time tumor and metastatic growth and angiogenesis and inhibition by representative drugs can be imaged and quantified for rapid antitumor, antimetastatic, and antiangiogenesis drug screening. The ***GFP*** -transfected tumor cells enabled a fundamental advance in the visualization of tumor growth and metastasis in real time in vivo.

L7 ANSWER 5 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:152084 BIOSIS
DN PREV200200152084
TI Myc-driven lymphomas respond with both apoptosis and senescence to anticancer treatment in vivo.
AU Schmitt, Clemens A. (1); Yang, Meng; Fridman, Jordan S.; Baranov, Euguge; Hoffman, Robert M.; Lowe, Scott W.
CS (1) Max-Delbruck-Center for Molecular Medicine, Hematology/Oncology, Charite, Humboldt-University, Campus Virchow Hospital, Berlin Germany
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 2, pp. 172b. http://www.bloodjournal.org/. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 2 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971.
DT Conference
LA English
AB Apoptosis and premature senescence are fundamental tumor suppressor programs against oncogene-mediated transformation. For example, oncogenic ras has been implicated in p16-mediated senescence while the c-myc oncogene promotes cell death, mainly in a p53-dependent manner. In turn, either program can become a mutational target depending on the driving oncogene. In fact, mutations of p53 or the INK4a/ARF locus, encoding p16 and the p53 regulator ARF, are common events in most tumor entities. Moreover, since many anticancer agents induce apoptosis, apoptotic defects may contribute to chemoresistance. Using the Emu-myc transgenic mouse lymphoma model, we examined to what extent genetic defects in the INK4a/ARF and p53 loci impair drug-induced long-term cell cycle arrest and apoptosis in myc-driven B-cell lymphomas in vivo. Myc-transgenic mice with heterozygous targeted disruption of either the ARF, the INK4a/ARF or the p53 locus rapidly develop lymphomas which are typically null for the respective loci due to loss of heterozygosity (LOH). Consequently, these tumors display apoptotic defects. Competitive introduction of the anti-apoptotic bcl-2 gene into ARF+/-, INK4a/ARF+/- or p53+/- myc-transgenic hematopoietic stem cells is sufficient to establish lymphomas without LOH. However, when treated with cyclophosphamide in vivo, ARF null lymphomas do not reproduce the poor response observed in INK4a/ARF null or p53 null lymphomas, but are prone to a reciprocal LOH of the retained INK4a allele (which encodes p16). While INK4a/ARF null or p53 null lymphomas progress quickly to a terminal stage upon treatment failure, control lymphomas (i.e. myc-driven lymphomas without a targeted lesion) engineered to harbor solely a Bcl-2 mediated apoptotic defect fail to achieve remissions, but remain stable over weeks as assessed by clinical observation and ***whole*** ***body*** ***imaging*** of living animals bearing ***GFP*** -tagged lymphomas. Proliferation markers indicate that those lymphomas respond to cyclophosphamide with a long-term cell cycle arrest. This arrest is associated with prolonged upregulation of both p53 and p16 protein levels. However, only control lymphomas turn positive for the senescence associated beta-galactosidase (SA-beta-Gal) activity within days after treatment, while p53 null lymphomas - despite high p16 protein levels - fail to arrest and to display SA-beta-Gal activity in situ. Therefore, p16 controls a p53-mediated senescence-like arrest program in myc-driven lymphomas upon DNA damaging treatment in vivo. These findings provide important insights into the genetic links between tumorigenesis and chemoresistance: ARF mutations disabling Myc signaling to p53, for example, disrupt a central tumor suppressor mechanism, but unlike mutations in p53, which controls both apoptosis and arrest, cannot co-select for resistance to drug-induced senescence.

L7 ANSWER 6 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
4
AN 2001:12806 BIOSIS
DN PREV200100012806
TI Visualizing gene expression by ***whole*** - ***body*** fluorescence ***imaging*** .
AU Yang, Meng; Baranov, Eugene; Moossa, A. R.; Penman, Sheldon; Hoffman, Robert M. (1)
CS (1) AntiCancer, Inc., 7917 Ostrow Street, San Diego, CA, 92111: all@anticancer.com USA
SO Proceedings of the National Academy of Sciences of the United States of America, (October 24, 2000) Vol. 97, No. 22, pp. 12278-12282. print.
ISSN: 0027-8424.
DT Article
LA English
SL English
AB Transgene expression in intact animals now can be visualized by noninvasive techniques. However, the instruments and protocols developed so far have been formidable and expensive. We describe here a system for rapidly visualizing transgene expression in major organs of intact live mice that is simple, rapid, and eminently affordable. Green fluorescent protein (***GFP***) is expressed in the cells of brain, liver, pancreas, prostate, and bone, and its fluorescence is encoded in ***whole*** - ***body*** optical ***images*** . For low-magnification images, animals are illuminated atop a fluorescence light box and directly viewed with a thermoelectrically cooled color charge-coupled device camera. Higher-magnification images are made with the camera focused through an epi-fluorescence dissecting microscope. Both nude and normal mice were labeled by directly injecting 8 X 1010 plaque-forming units/ml of adenoviral ***GFP*** in 20-100 mul PBS and 10% glycerol into either the brain, liver, pancreas, prostate, or bone marrow. Within 5-8 h after adenoviral ***GFP*** injection, the fluorescence of the expressed ***GFP*** in brain and liver became visible, and ***whole*** - ***body*** ***images*** were recorded at video rates. The ***GFP*** fluorescence continued to increase for at least 12 h and remained detectable in liver for up to 4 months. The system's rapidity of image acquisition makes it capable of real-time recording. It requires neither exogenous contrast agents, radioactive substrates, nor long processing times. The method requires only that the expressed gene or promoter be fused or operatively linked to ***GFP*** . A comparatively modest investment allows the study of the therapeutic and diagnostic potential of suitably tagged genes in relatively opaque organisms.

L7 ANSWER 7 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
5
AN 2000:151951 BIOSIS
DN PREV200000151951
TI ***Whole*** - ***body*** optical ***imaging*** of green fluorescent protein-expressing tumors and metastases.
AU Yang, Meng; Baranov, Eugene; Jiang, Ping; Sun, Fang-Xian; Li, Xiao-Ming; Li, Lingna; Hasegawa, Satoshi; Bouvet, Michael; Al-Tuwaijri, Maraya; Chishima, Takashi; Shimada, Hiroshi; Moossa, A. R.; Penman, Sheldon; Hoffman, Robert M. (1)
CS (1) AntiCancer, Inc., 7917 Ostrow Street, San Diego, CA, 92111 USA
SO Proceedings of the National Academy of Sciences of the United States of America., (Feb. 1, 2000) Vol. 97, No. 3, pp. 1206-1211.
ISSN: 0027-8424.
DT Article
LA English
SL English
AB We have imaged, in real time, fluorescent tumors growing and metastasizing in live mice. The ***whole*** - ***body*** optical ***imaging*** system is external and noninvasive. It affords unprecedented continuous visual monitoring of malignant growth and spread within intact animals. We have established new human and rodent tumors that stably express very high levels of the Aequorea victoria green fluorescent protein (***GFP***) and transplanted these to appropriate animals. B16F0- ***GFP*** mouse melanoma cells were injected into the tail vein or portal vein of 6-week-old C57BL/6 and nude mice. ***Whole*** - ***body*** optical ***images*** showed metastatic lesions in the brain, liver, and bone of B16F0- ***GFP*** that were used for real time, quantitative measurement of tumor growth in each of these organs. The AC3488- ***GFP*** human colon cancer was surgically implanted orthotopically into nude mice. ***Whole*** - ***body*** optical ***images*** showed, in real time, growth of the primary colon tumor and its metastatic lesions in the liver and skeleton. Imaging was with either a trans-illuminated epifluorescence microscope or a fluorescence light box and thermoelectrically cooled color charge-coupled device camera. The depth to which metastasis and micrometastasis could be imaged depended on their size. A 60-mum diameter tumor was detectable at a depth of 0.5 mm whereas a 1,800-mum tumor could be visualized at 2.2-mm depth. The simple, noninvasive, and highly selective imaging of growing tumors, made possible by strong ***GFP*** fluorescence, enables the detailed imaging of tumor growth and metastasis formation. This should facilitate studies of modulators of cancer growth including inhibition by potential chemotherapeutic agents.

L7 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2002 ACS
AN 2000:516147 CAPLUS
DN 134:144026
TI External optical imaging of freely moving mice with green fluorescent protein-expressing metastatic tumors
AU Yang, Meng; Baranov, Eugene; Shimada, Hiroshi; Moossa, A. R.; Hoffman, Robert M.
CS AntiCancer, Inc., San Diego, CA, USA
SO Proceedings of SPIE-The International Society for Optical Engineering (2000), 3921(Optical Diagnostics of Living Cells III), 256-259
CODEN: PSISDG; ISSN: 0277-786X

PB SPIE-The International Society for Optical Engineering
DT Journal
LA English
AB We report here a new approach to genetically engineering tumors to become fluorescence such that they can be imaged externally in freely-moving animals. We describe here external high-resoln. real-time fluorescent optical imaging of metastatic tumors in live mice. Stable high-level green fluorescent protein (***GFP***)-expressing human and rodent cell lines enable tumors and metastasis is formed from them to be externally imaged from freely-moving mice. Real-time tumor and metastatic growth were quantitated from ***whole*** - ***body*** real-time ***imaging*** in ***GFP*** -expressing melanoma and colon carcinoma models. This ***GFP*** optical imaging system is highly appropriate for high throughput in vivo drug screening.
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:300206 BIOSIS
DN PREV200100300206
TI Visualizing leukemia & lymphoma cell homing and quantification of tumor burden in response to therapy in living animals.
AU Edinger, Matthias (1); Verneris, Michael R. (1); Cao, Yuan (1); Bachmann, Michael H. (1); Costa, Gina L. (1); Contag, Christopher H. (1); Negrin, Robert S. (1)
CS (1) Departments of Medicine and Pediatrics, Stanford University, School of Medicine, Stanford, CA USA
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 123a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DT Conference
LA English
SL English
AB Revealing the mechanisms of neoplastic disease and enhancing our ability to intervene in these processes requires an increased understanding of cellular and molecular changes as they occur in living animals. We have previously shown, that since light is transmitted through mammalian tissues at a low level, we can detect light emission from tumor cells that express luciferase from within living animals, using low light imaging cameras. To establish animal models of leukemia and lymphoma, we used the A20 and Bcl1 lymphoma cell lines. A20 cells were transfected with the pCDNA3.1-luc plasmid containing a modified luciferase gene (A20-luc). Using light emission as an indicator, tumor engraftment, exponential growth and rejection was followed in individual animals after sc, iv and ip injections. Tumor engraftment in spleen, liver and lymph nodes could be localized. As few as 103 A20-luc cells could be detected after sc injection. Following iv injection of 104 A20-luc cells in a syngeneic BMT model, leukemic disease was observed with tumor infiltration of the femurs, humeri, sternum, vertebrae and skull. A retroviral transduction system was used to transfer the gene for a ***GFP*** /luc fusion protein to the Bcl1 lymphoma, known to localize to liver and spleen. ***GFP*** expressing cells were sorted by FACS and injected into mice iv. Initially, as few as 7000 tumor cells could be detected, and subsequently tumor engraftment in liver and spleen was observed. Tumor growth was followed over time and quantified from these internal organs. We also investigated the therapeutic application of cytotoxic cells termed cytokine induced killer cells (CIK) which co-express T cell and NK cell markers and are generated by in vitro expansion from splenocytes. Treatment of A20-luc tumor bearing animals with 107 CIK cells led to a decrease of tumor signal from sc growing tumors and 75% of the mice were cured within 2 wks. To examine trafficking of these activated T cells we used the retroviral transduction method to label the cells. After iv injection transduced cells were detected in the lungs, 12 h later they locate to liver and spleen, and generalize thereafter. We conclude, that ***whole*** ***body*** ***imaging*** of labeled tumor cells reveals patterns of systemic disease allowing visualization of minimal disease and therapeutic response. This will improve our insights in tumor biology, be useful in directing subsequent ex vivo assays, and provide a powerful tool to examine the kinetics of response to novel therapies.

L7 ANSWER 10 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:502217 BIOSIS
DN PREV200000487795
TI ***GFP*** tumor, metastasis and angiogenesis ***whole*** - ***body*** ***imaging*** .
AU Yang, M. (1); Baranov, E. (1); Jiang, P. (1); Sun, F.-X. (1); Li, L. (1); Hasegawa, S.; Al-Tuwaijri, M.; Shimada, H.; Moossa, A. R.; Hoffman, R. (1)
CS (1) AntiCancer, Inc., San Diego, CA, 92111 USA
SO Clinical & Experimental Metastasis, (1999) Vol. 17, No. 9, pp. 747. print.
Meeting Info.: VIII International Congress of the Metastasis Research Society London, UK September 24-27, 2000
ISSN: 0262-0898.
DT Conference
LA English
SL English

=> d his

(FILE 'HOME' ENTERED AT 18:58:33 ON 08 MAY 2002)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 18:58:42 ON 08 MAY 2002
L1 870 S WHOLE BODY IMAG?
L2 109 S L1 AND FLUOR?
L3 13 S L1 AND (GFP OR EGFP OR BFP OR RFP)
L4 7 DUP REM L3 (6 DUPLICATES REMOVED)
L5 1836 S WHOLE BODY (3A)IMAG?
L6 19 S L5 AND (GFP OR EGFP OR BFP OR RFP)
L7 10 DUP REM L6 (9 DUPLICATES REMOVED)

=> s l1 and lucifer?
L8 8 L1 AND LUCIFER?

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9 6 DUP REM L8 (2 DUPLICATES REMOVED)

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YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L9 ANSWER 1 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:252653 BIOSIS
DN PREV200200252653
TI Alternatives to animal testing in microbiology and infectiology.
AU Bottrill, K. (1); Combes, R. D.
CS (1) FRAME, 96-98 N. Sherwood Street, Russell and Burch House, Nottingham,
NG1 4EE: krys@frame-uk.demon.co.uk UK
SO Schmidt, Axel [Editor]; Weber, Olaf F. [Editor]. Contributions to Microbiology, (2001) Vol. 9, pp. 89-117. Contributions to Microbiology.
Animal testing in infectiology. print.
Publisher: S. Karger Publishers Inc. 79 Fifth Avenue, New York, NY, 10003, USA.
ISSN: 1420-9519. ISBN: 3-8055-7260-3 (cloth).
DT Book
LA English

L9 ANSWER 2 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 2001:554953 BIOSIS
DN PREV200100554953
TI Rapid in vivo functional analysis of transgenes in mice using ***whole*** ***body*** ***imaging*** of ***luciferase*** expression.
AU Zhang, Weisheng; Feng, Jian Q.; Harris, Stephen E.; Contag, Pamela R.; Stevenson, David K.; Contag, Christopher H. (1)
CS (1) Division of Neonatal and Developmental Medicine, Departments of Pediatrics, and Microbiology and Immunology, Stanford University Medical Center, Stanford University, Stanford, CA, 94305-5208: ccontag@cmgm.stanford.edu USA
SO Transgenic Research, (October, 2001) Vol. 10, No. 5, pp. 423-434. print.
ISSN: 0962-8819.
DT Article
LA English
SL English
AB The use of transgenic animals in biomedical research is increasing rapidly and may be the best means of determining gene function. Generating transgenic animals typically requires time-consuming screening processes, and gene function is assessed by an array of difficult phenotypic and biochemical assays performed ex vivo. To address the unmet need in transgenic research for functional assays performed with ease in living animals, we demonstrate here that in vivo detection of ***luciferase*** enzyme as a transcriptional reporter facilitates rapid screening for both the presence and function of transgenes in intact living mice. Using this approach we identified three bioluminescent transgenic founders where the transgene consisted of the heme oxygenase promoter fused to the modified coding sequence of the ***luciferase*** gene. These founders were identified from 183 pups and confirmed by PCR analysis. Identification of HO-1-luc homozygotes from back-crossed F2 littermates was then accelerated by in vivo imaging. In another transgenic mouse line, where the transgene was comprised of the bone morphogenic-4 (BMP4) promoter fused to the modified ***luciferase*** gene, we were able to identify transgenic animals and in each line we were able to visualize patterns of expression in living animals over time. The light production from these transgenic mice indicated that the desired DNA fragment was functional and different expression profiles apparent at different ages and after gene induction.

L9 ANSWER 3 OF 6 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 2
AN 2001201957 EMBASE
TI In utero delivery of adeno-associated viral vectors: Intraperitoneal gene transfer produces long-term expression.
AU Lipshutz G.S.; Gruber C.A.; Cao Y.-A.; Hardy J.; Contag C.H.; Gaensler K.M.L.
CS K.M.L. Gaensler, Department of Medicine, University of California, 3rd and Parnassus Avenues, San Francisco, CA 94143-0793, United States. nintim@itsa.ucsf.edu
SO Molecular Therapy, (2001) 3/3 (284-292).
Refs: 46
ISSN: 1525-0016 CODEN: MTOHCK

CY United States
DT Journal; Article
FS 004 Microbiology
022 Human Genetics
037 Drug Literature Index
039 Pharmacy
052 Toxicology
LA English
SL English
AB Recombinant adeno-associated viruses (rAAV) are promising gene transfer vectors that produce long-term expression without toxicity. To investigate future approaches for in utero gene delivery, the efficacy and safety of prenatal administration of rAAV were determined. Using ***luciferase*** as a reporter, expression was assessed by ***whole*** - ***body*** ***imaging*** and by analysis of ***luciferase*** activity in tissue extracts, at the time of birth and monthly thereafter. Transgene expression was detected in all injected animals. Highest levels of ***luciferase*** activity were detected at birth in the peritoneum and liver, while the heart, brain, and lung demonstrated low-level expression. In vivo ***luciferase*** imaging revealed persistent peritoneal expression for 18 months after in utero injection and provided a sensitive whole-body assay, useful in identifying tissues for subsequent analyses. There was no detectable hepatocellular injury. Antibodies that reacted with either ***luciferase*** or rAAV were not found. AAV sequences were not detected in germ-line tissues of injected animals or in tissues of their progeny. In utero AAV-mediated gene transfer in this animal model demonstrates that novel therapeutic vectors and strategies can be rapidly tested in vivo and that rAAV may be developed to ameliorate genetic diseases with perinatal morbidity and mortality.

L9 ANSWER 4 OF 6 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2002024178 EMBASE
TI In vivo patterns of heme oxygenase-1 transcription.
AU Contag C.H.; Stevenson D.K.
CS C.H. Contag, Div. of Neonatal and Devmtl. Med., Department of Pediatrics, Stanford University, Stanford, CA 94305-5208, United States
SO Journal of Perinatology, (2001) 21/SUPPL. 1 (S119-S124).
Refs: 14
ISSN: 0743-8346 CODEN: JOPEEI
CY United Kingdom
DT Journal; Conference Article
FS 022 Human Genetics
029 Clinical Biochemistry
007 Pediatrics and Pediatric Surgery
037 Drug Literature Index
030 Pharmacology
048 Gastroenterology
LA English
SL English
AB Gene fusions composed of specific promoters and bioluminescent reporter genes can be used to assess gene expression patterns using ***whole*** - ***body*** ***imaging*** in living animal models. A transgenic mouse model was developed using the regulatory elements of the heme oxygenase promoter to drive ***luciferase*** as the reporter gene. In these transgenic mice, heme oxygenase (HO)-1 expression was apparent in neuronal tissues of neonates but not adults as measured by ***whole*** - ***body*** ***imaging*** , and in adults transcription of the reporter gene was inducible by known inducers of HO-1 transcription. ***Whole*** - ***body*** ***imaging*** of ***luciferase*** activity was then used to evaluate the effects of metalloporphyrins (Mps) on the transcription of the reporter gene. Some of the Mps, which are potent inhibitors of HO activity, did not activate the reporter gene above background. These Mps are ideally suited as chemotherapeutics that may target bilirubin production rates by inhibiting HO activity, but not result in a net increase in output from the HO gene. In contrast, known inducers of HO transcription did increase ***luciferase*** activity as did some of the other Mps that have been examined. Using whole-body in vivo transcriptional assays may facilitate rapid screening of potential therapeutic compounds for both desired and untoward effects.

L9 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:300206 BIOSIS
DN PREV200100300206
TI Visualizing leukemia & lymphoma cell homing and quantification of tumor burden in response to therapy in living animals.
AU Edinger, Matthias (1); Verneris, Michael R. (1); Cao, Yuan (1); Bachmann, Michael H. (1); Costa, Gina L. (1); Contag, Christopher H. (1); Negrin, Robert S. (1)
CS (1) Departments of Medicine and Pediatrics, Stanford University, School of Medicine, Stanford, CA USA
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 123a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DT Conference
LA English
SL English
AB Revealing the mechanisms of neoplastic disease and enhancing our ability to intervene in these processes requires an increased understanding of cellular and molecular changes as they occur in living animals. We have previously shown, that since light is transmitted through mammalian tissues at a low level, we can detect light emission from tumor cells that express ***luciferase*** from within living animals, using low light imaging cameras. To establish animal models of leukemia and lymphoma, we used the A20 and Bcl1 lymphoma cell lines. A20 cells were transfected with the pCDNA3.1-luc plasmid containing a modified ***luciferase*** gene (A20-luc). Using light emission as an indicator, tumor engraftment, exponential growth and rejection was followed in individual animals after sc, iv and ip injections. Tumor engraftment in spleen, liver and lymph nodes could be localized. As few as 103 A20-luc cells could be detected after sc injection. Following iv injection of 104 A20-luc cells in a syngeneic BMT model, leukemic disease was observed with tumor infiltration of the femurs, humeri, sternum, vertebrae and skull. A retroviral transduction system was used to transfer the gene for a GFP/luc fusion protein to the Bcl1 lymphoma, known to localize to liver and spleen. GFP expressing cells were sorted by FACS and injected into mice iv. Initially, as few as 7000 tumor cells could be detected, and subsequently tumor engraftment in liver and spleen was observed. Tumor growth was followed over time and quantified from these internal organs. We also investigated the therapeutic application of cytotoxic cells termed cytokine induced killer cells (CIK) which co-express T cell and NK cell markers and are generated by in vitro expansion from splenocytes. Treatment of A20-luc tumor bearing animals with 107 CIK cells led to a decrease of tumor signal from sc growing tumors and 75% of the mice were cured within 2 wks. To examine trafficking of these activated T cells we used the retroviral transduction method to label the cells. After iv injection transduced cells were detected in the lungs, 12 h later they locate to liver and spleen, and generalize thereafter. We conclude, that ***whole*** ***body*** ***imaging*** of labeled tumor cells reveals patterns of systemic disease allowing visualization of minimal disease and therapeutic response. This will improve our insights in tumor biology, be useful in directing subsequent ex vivo assays, and provide a powerful tool to examine the kinetics of response to novel therapies.

L9 ANSWER 6 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:59876 BIOSIS
DN PREV200000059876
TI Noninvasive assessment of tumor cell proliferation in animal models.
AU Edinger, Matthias; Sweeney, Thomas J.; Tucker, Amanda A.; Olomu, Adesuwa
B.; Negrin, Robert S.; Contag, Christopher H. (1)
CS (1) School of Medicine, Stanford University, Stanford, CA USA
SO Neoplasia (New York), (Oct., 1999) Vol. 1, No. 4, pp. 303-310.
ISSN: 1522-8002.
DT Article
LA English
SL English
AB Revealing the mechanisms of neoplastic disease and enhancing our ability to intervene in these processes requires an increased understanding of cellular and molecular changes as they occur in intact living animal models. We have begun to address these needs by developing a method of labeling tumor cells through constitutive expression of an optical reporter gene, and noninvasively monitoring cellular proliferation in vivo using a sensitive photon detection system. A stable line of HeLa cells that expressed a modified firefly ***luciferase*** gene was generated, and proliferation of these cells in irradiated severe combined immunodeficiency (SCID) mice was monitored. Tumor cells were introduced into animals via subcutaneous, intraperitoneal and intravenous inoculation and ***whole*** ***body*** ***images*** , that revealed tumor location and growth kinetics, were obtained. The number of photons that were emitted from the labeled tumor cells and transmitted through murine tissues was sufficient to detect 1 X 103 cells in the peritoneal cavity, 1 X 104 cells at subcutaneous sites and 1 X 106 circulating cells immediately following injection. The kinetics of cell proliferation, as measured by photon emission, was exponential in the peritoneal cavity and at subcutaneous sites. Intravenous inoculation resulted in detectable colonies of tumor cells in animals receiving more than 1 X 106 cells. Our demonstrated ability to detect small numbers of tumor cells in living animals noninvasively suggests that therapies designed to treat minimal disease states, as occur early in the disease course and after elimination of the tumor mass, may be monitored using this approach. Moreover, it may be possible to monitor micrometastases and evaluate the molecular steps in the metastatic process. Spatiotemporal analyses of neoplasia will improve the predictability of animal models of human disease as study groups can be followed over time, and this method will accelerate development of novel therapeutic strategies.

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(FILE 'HOME' ENTERED AT 18:58:33 ON 08 MAY 2002)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 18:58:42 ON 08 MAY 2002
L1 870 S WHOLE BODY IMAG?
L2 109 S L1 AND FLUOR?
L3 13 S L1 AND (GFP OR EGFP OR BFP OR RFP)
L4 7 DUP REM L3 (6 DUPLICATES REMOVED)
L5 1836 S WHOLE BODY (3A)IMAG?
L6 19 S L5 AND (GFP OR EGFP OR BFP OR RFP)
L7 10 DUP REM L6 (9 DUPLICATES REMOVED)
L8 8 S L1 AND LUCIFER?
L9 6 DUP REM L8 (2 DUPLICATES REMOVED)

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PROCESSING COMPLETED FOR L2
L10 82 DUP REM L2 (27 DUPLICATES REMOVED)

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L11 311 L5 AND FLUOR?

=> dup rem l11
PROCESSING COMPLETED FOR L11
L12 242 DUP REM L11 (69 DUPLICATES REMOVED)

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1 FILES SEARCHED...
L13 191 L12 AND PY<=2000

=> d bib abs 1-10

L13 ANSWER 1 OF 191 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:93422 BIOSIS
DN PREV200200093422
TI [Assessment of positron emission tomography in oncology. Original Title: Aplicaciones de la tomografia de emission de positrones (PET) en oncologia..
AU Palazzo, Felipe Salvador (1)
CS (1) Instituto de Oncologia "Angel H. Roffo", Facultad de Medicina, UBA, Av. San Martin 5481, C1417DTB, Buenos Aires Argentina
SO Prensa Medica Argentina, (***Diciembre, 2000***) Vol. 87, No. 10, pp. 1024-1036. print.
ISSN: 0032-745X.
DT General Review
LA Spanish
AB Positron emission tomography (PET) is one of the most promising diagnostic procedures in oncology. Using the glucose analogue ***fluorodeoxyglucose*** , PET produces ***whole*** . ***body*** ***images*** and is highly sensitive for tumor diagnosis and staging. Besides, image registration yields anatomo-metabolic information that could be used in a lot of additional situation. We review typical and specific clinical situations in which PET-FDG has proven not only its diagnostic accuracy, but also its impact on patient management, i.e., the staging of non-small cell lung cancer; diagnosis and staging of colo-rectal cancer and head and neck cancer recurrence.

L13 ANSWER 2 OF 191 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:318396 BIOSIS
DN PREV200100318396
TI Prognostic value of whole body FDG/PET scanning in multiple myeloma.
AU Durie, Brian G. M. (1); Waxman, Alan; D'Agnolo, Alessandro
CS (1) Cancer Center, Cedars, Sinai Medical Center, Los Angeles, CA USA
SO Blood, (***November 16, 2000***) Vol. 96, No. 11 Part 1, pp. 836a-837a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DT Conference
LA English
SL English
AB The purpose of this study was to evaluate the clinical utility of whole body positron emission tomography with ***fluorodeoxyglucose*** (FDG/PET) in patients with multiple myeloma and related monoclonal diseases. Between July 1996 and July 2000, 66 patients underwent 98 FDG/PET scans with 25 patients having 2 or more scans. Results were compared with routine clinical and staging information including computer tomography (CT) and MRI scans as indicated. Of the 66 patients: 16 had previously untreated active myeloma, 13 had monoclonal gammopathy of undetermined significance (MGUS), 9 were in remission and 26 had relapsing disease. Negative whole body FDG/PET reliably predicted stable MGUS. All 13 MGUS patients remain without disease progression at 3-43 months. Conversely, previously untreated (PU) patients with active myeloma had focal and/or diffusely positive scans. 4/16 (25%) PU patients with positive FDG/PET scans had negative full radiologic surveys. Another 4/16 (25%) patients had focal extra medullary disease. This was confirmed by biopsy and/or other imaging techniques. Extra medullary uptake also occurred in 6/26 (23%) relapse patients. This extra medullary uptake was a very poor prognostic factor both pretreatment and at relapse - e.g., post transplant relapse at 3-6 months. Persistant positive FDG/PET predicted early relapse. 13/16 (50%) relapsing patients had new sites of disease identified. The FDG/PET scan results were especially helpful in identifying focal recurrent disease in patients with nonsecretory or hyposecretory disease amenable to local irradiation therapy used in 6 patients. Negative FDG/PET results predicted stable remission (6-42 months). Focal relapse was confirmed by biopsy and/or other ***imaging*** . In conclusion, ***whole*** ***body*** FDG/PET ***imaging*** provides important prognostic information which is clinically useful in the evaluation of plasma cell disorders. Both pretreatment staging and serial monitoring are enhanced. Formal cost effectiveness analysis is recommended.

L13 ANSWER 3 OF 191 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:300206 BIOSIS
DN PREV200100300206
TI Visualizing leukemia & lymphoma cell homing and quantification of tumor burden in response to therapy in living animals.
AU Edinger, Matthias (1); Verneris, Michael R. (1); Cao, Yuan (1); Bachmann, Michael H. (1); Costa, Gina L. (1); Contag, Christopher H. (1); Negrin, Robert S. (1)
CS (1) Departments of Medicine and Pediatrics, Stanford University, School of Medicine, Stanford, CA USA
SO Blood, (***November 16, 2000***) Vol. 96, No. 11 Part 1, pp. 123a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DT Conference
LA English
SL English
AB Revealing the mechanisms of neoplastic disease and enhancing our ability to intervene in these processes requires an increased understanding of cellular and molecular changes as they occur in living animals. We have previously shown, that since light is transmitted through mammalian tissues at a low level, we can detect light emission from tumor cells that express luciferase from within living animals, using low light imaging cameras. To establish animal models of leukemia and lymphoma, we used the A20 and Bcl1 lymphoma cell lines. A20 cells were transfected with the pCDNA3.1-luc plasmid containing a modified luciferase gene (A20-luc). Using light emission as an indicator, tumor engraftment, exponential growth and rejection was followed in individual animals after sc, iv and ip injections. Tumor engraftment in spleen, liver and lymph nodes could be localized. As few as 103 A20-luc cells could be detected after sc injection. Following iv injection of 104 A20-luc cells in a syngeneic BMT model, leukemic disease was observed with tumor infiltration of the femurs, humeri, sternum, vertebrae and skull. A retroviral transduction system was used to transfer the gene for a GFP/luc fusion protein to the Bcl1 lymphoma, known to localize to liver and spleen. GFP expressing cells were sorted by FACS and injected into mice iv. Initially, as few as 7000 tumor cells could be detected, and subsequently tumor engraftment in liver and spleen was observed. Tumor growth was followed over time and quantified from these internal organs. We also investigated the therapeutic application of cytotoxic cells termed cytokine induced killer cells (CIK) which co-express T cell and NK cell markers and are generated by in vitro expansion from splenocytes. Treatment of A20-luc tumor bearing animals with 107 CIK cells led to a decrease of tumor signal from sc growing tumors and 75% of the mice were cured within 2 wks. To examine trafficking of these activated T cells we used the retroviral transduction method to label the cells. After iv injection transduced cells were detected in the lungs, 12 h later they locate to liver and spleen, and generalize thereafter. We conclude, that ***whole*** ***body*** ***imaging*** of labeled tumor cells reveals patterns of systemic disease allowing visualization of minimal disease and therapeutic response. This will improve our insights in tumor biology, be useful in directing subsequent ex vivo assays, and provide a powerful tool to examine the kinetics of response to novel therapies.

L13 ANSWER 4 OF 191 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:65365 BIOSIS
DN PREV200100065365
TI Glucose uptake by individual skeletal muscles during running using whole-body positron emission tomography.
AU Fujimoto, Toshihiko (1); Itoh, Masatoshi; Tashiro, Manabu; Yamaguchi, Keiichiro; Kubota, Kazuo; Ohmori, Hiroaki
CS (1) Department of Medicine and Science in Sports and Exercise, Graduate School of Medicine, Tohoku University, Kawauchi Aobaku, Sendai, 980-8576: fujimoto@mail.cc.tohoku.ac.jp Japan
SO European Journal of Applied Physiology, (***November, 2000***) Vol. 83, No. 4-5, pp. 297-302. print.
ISSN: 1439-6319.
DT Article
LA English
SL English
AB The purpose of this study was to examine, by positron emission tomography (PET), the distribution of (18F) ***fluoro*** -deoxy-glucose ((18F)FDG) uptake by human muscles during 35 min of running. Thirteen healthy male subjects were studied, seven of whom participated in the exercise study. Running intensity was kept constant such that the subjects' heart rates were maintained at between 140 and 150 beats per minute. (18F)FDG (62.9 (14.8) MBq, mean (SD)) was injected after 15 min of running. PET imaging was started immediately after the running ended. The ratio of (18F)FDG uptake by muscles in runners to that in control subjects (r-c ratio) varied from three to six for the muscles of the foot and leg below the knee joint. The r-c ratio of the medial head of the gastrocnemius (MG) was higher than that of its lateral head (LG). The r-c ratio of the rectus femoris (RF) was lower than that of the other three muscles of the quadriceps femoris (QF). The r-c ratio of inactive muscles located above the waist was approximately 0.7. These results suggest that, during the moderate running of this study: (1) glucose uptake by muscles of the foot and leg below the knee joint clearly increases, (2) the r-c ratio differs significantly among the skeletal muscles, which act synergistically, and (3) glucose uptake by inactive skeletal muscles decreases.

L13 ANSWER 5 OF 191 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2001:12806 BIOSIS
DN PREV200100012806
TI Visualizing gene expression by ***whole*** - ***body*** ***fluorescence*** ***imaging*** .
AU Yang, Meng; Baranov, Eugene; Moossa, A. R.; Penman, Sheldon; Hoffman, Robert M. (1)
CS (1) AntiCancer, Inc., 7917 Ostrow Street, San Diego, CA, 92111: all@anticancer.com USA
SO Proceedings of the National Academy of Sciences of the United States of America, (***October 24, 2000***) Vol. 97, No. 22, pp. 12278-12282. print.
ISSN: 0027-8424.
DT Article
LA English
SL English
AB Transgene expression in intact animals now can be visualized by noninvasive techniques. However, the instruments and protocols developed so far have been formidable and expensive. We describe here a system for rapidly visualizing transgene expression in major organs of intact live mice that is simple, rapid, and eminently affordable. Green ***fluorescent*** protein (GFP) is expressed in the cells of brain, liver, pancreas, prostate, and bone, and its ***fluorescence*** is encoded in ***whole*** - ***body*** optical ***images*** . For low-magnification images, animals are illuminated atop a ***fluorescence*** light box and directly viewed with a thermoelectrically cooled color charge-coupled device camera. Higher-magnification images are made with the camera focused through an epi- ***fluorescence*** dissecting microscope. Both nude and normal mice were labeled by directly injecting 8 X 1010 plaque-forming units/ml of adenoviral GFP in 20-100 mul PBS and 10% glycerol into either the brain, liver, pancreas, prostate, or bone marrow. Within 5-8 h after adenoviral GFP injection, the ***fluorescence*** of the expressed GFP in brain and liver became visible, and ***whole*** - ***body*** ***images*** were recorded at video rates. The GFP ***fluorescence*** continued to increase for at least 12 h and remained detectable in liver for up to 4 months. The system's rapidity of image acquisition makes it capable of real-time recording. It requires neither exogenous contrast agents, radioactive substrates, nor long processing times. The method requires only that the expressed gene or promoter be fused or operatively linked to GFP. A comparatively modest investment allows the study of the therapeutic and diagnostic potential of suitably tagged genes in relatively opaque organisms.

L13 ANSWER 6 OF 191 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:518626 BIOSIS
DN PREV200000518626
TI FDG PET and immunoscintigraphy with 99mTc-labeled antibody fragments for detection of the recurrence of colorectal carcinoma.
AU Willkomm, Petra (1); Bender, Hans; Bangard, Michael; Decker, Pan; Gruenwald, Frank; Biersack, Hans-Juergen
CS (1) Department of Nuclear Medicine, Sigmund-Freud-Str. 25, D-53127, Bonn Germany
SO Journal of Nuclear Medicine, (***October, 2000***) Vol. 41, No. 10, pp. 1657-1663. print.
ISSN: 0161-5505.
DT Article
LA English
SL English
AB The aim of this study was to compare FDG PET with a new monoclonal antibody-based imaging agent that comprises an anti-carcinoembryonic antigen (CEA) monoclonal antibody Fab' fragment directly labeled with 99mTc. Methods: Twenty-eight patients who were previously treated for colorectal carcinoma and in whom recurrence was suspected were examined with FDG PET and immunoscintigraphy. The most common indications were an elevation of serum CEA (13 patients), suggestive lesions documented by CT (9 patients), sonography (4 patients), and severe constipation (2 patients). Planar imaging and SPECT were performed 4-6 h after intravenous injection of the new ***imaging*** agent. ***Whole*** - ***body*** PET was performed 45-60 min after intravenous injection of FDG. The findings were confirmed by conventional diagnostic modalities, surgery, and histology. Results: Histology confirmed local tumor recurrence in 9 of 28 patients. Clinical follow-up or CT confirmed the presence of liver metastases in 9 patients and lymph node involvement, lung metastases, and bone metastases in 2 patients each. The new agent correctly detected 8 of 9 local recurrences, whereas FDG PET was able to detect all 9 cases and in 1 case was false-positive. Liver metastases were confirmed in 9 patients by FDG PET but in only 1 patient by the new agent. Two cases with lymph node metastases and 2 cases with lung metastases were correctly identified by FDG PET, but none were detected by the new agent. Finally, bone metastases were identified in 1 patient by FDG PET but not with the new agent, whereas bone marrow infiltration (n = 1) was diagnosed by both imaging modalities. Conclusion: These results indicate that FDG PET and 99mTc-labeled anti-CEA Fab' are suitable for the diagnosis of local recurrence of colorectal carcinoma but that FDG PET is clearly superior in the detection of distant metastases (liver, bone, and lung) and lymph node involvement.

L13 ANSWER 7 OF 191 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:431880 BIOSIS
DN PREV200000431880
TI ***Whole*** ***body*** positron emission tomography ***imaging*** of activated lymphoid tissues during acute simian-human immunodeficiency virus 89.6PD infection in rhesus macaques.
AU Wallace, Marianne; Pyzalski, Robert; Horejsh, Douglas; Brown, Charles; Djavani, Mahmoud; Lu, Yichen; Hanson, Joan M.; Mitchen, Jacque L.; Perlman, Scott B.; Pauza, C. David (1)
CS (1) Institute of Human Virology, Baltimore, MD, 21201 USA
SO Virology, (***September 1, 2000***) Vol. 274, No. 2, pp. 255-261. print.
ISSN: 0042-6822.
DT Article
LA English
SL English
AB Mechanisms of acute retroviral pathogenesis have been examined during primary infection of rhesus macaques with simian-human immunodeficiency virus 89.6PD (SHIV89.6PD). During acute infection, between initial exposure and establishment of antigen-specific immune responses that stabilize the virus burden, rapid immune system changes influence the viral set-point and dictate subsequent steps in disease progression. In a previous study, we described specific patterns of lymphocyte activation during acute SHIV89.6PD infection. We now extend these studies to describe lymphoid tissue activation, using whole body positron emission tomography (PET) and the radioactive tracer 2-(18F) ***fluorodeoxyglucose*** (FDG). Within a few days after primary infection by intravenous, intrarectal, or intravaginal routes, PET-FDG imaging revealed a distinct pattern of lymphoid tissue activation centered on axillary, cervical, and mediastinum lymph nodes. Increased tissue FDG uptake preceded fulminant virus replication at these sites, suggesting that a diffusible factor of host or viral origin was responsible for lymphoid tissue changes. These data show that activation of lymphoid tissues in the upper body is an early response to virus infection and that diffusible mediators of activation might be important targets for vaccine or therapeutic intervention strategies.

L13 ANSWER 8 OF 191 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:412220 BIOSIS
DN PREV200000412220
TI Use of a coincidence gamma camera to detect primary tumor with 18fluoro-2-deoxy-glucose in cervical lymph node metastases from an unknown origin.
AU Perie, Sophie (1); Talbot, Jean-Noel; Monceaux, Guy; Grahek, Dany; Kerrou, Khaldoun; Montravers, Francoise; St Guily, Jean Lacau
CS (1) Service d'Oto-Rhino-Laryngologie et Chirurgie de la Face et du Cou, Hopital Tenon, 4, rue de la Chine, 75020, Paris France
SO Annals of Otology Rhinology & Laryngology, (***August, 2000***) Vol. 109, No. 8 Part 1, pp. 755-760. print.
ISSN: 0003-4894.
DT Article
LA English
SL English
AB This study was performed to evaluate the ability of a dual-head gamma camera with 18fluoro-2-deoxy-glucose coincidence detection emission tomography (FDG-CDET) to detect primary tumors in patients with cervical lymph node metastases of head and neck squamous cell carcinoma from an unknown origin. From 60 patients with untreated head and neck squamous cell carcinoma, we selected 4 in whom no evidence of the primary's origin was found by the conventional methods used for the evaluation of head and neck tumors. In addition to the panendoscopy, chest radiography, a computed tomography (CT) scan, and FDG-CDET were performed. Both FDG-CDET and the CT scan located cervical lymph node metastases. In addition, FDG-CDET located the primary tumor in 3 of the 4 patients, and the tumors were confirmed with histopathologic findings. In contrast, the CT scan detected the primary tumor in none of them. FDG tomography performed on a coincidence gamma camera appears to be a successful new tool in detecting occult primary tumors in head and neck carcinoma, and is useful in guiding endoscopic biopsies. It has, further, the important potential ability to detect distant metastases on ***whole*** ***body*** ***images*** .

L13 ANSWER 9 OF 191 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:402588 BIOSIS
DN PREV200000402588
TI Prostate cancer: The contribution of nuclear medicine.
AU Britton, K. E. (1); Feneley, M. R.; Jan, H.; Chengazi, V. U.; Granowska, M.
CS (1) Department of Nuclear Medicine, St Bartholomew's Hospital, London, EC1A 7BE UK
SO BJU International, (***July, 2000***) Vol. 86, No. Supplement 1, pp. 135-142. print.
ISSN: 1464-4096.
DT Article
LA English
SL English

L13 ANSWER 10 OF 191 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:287230 BIOSIS
DN PREV200000287230
TI Significance of PET-FDG in comparison with 131I WBS and serum Tg in detection of recurrent and metastatic papillary thyroid carcinoma.
AU Hoda, S. (1); Ardakani, N. (1); Hawkins, R. A. (1)

CS (1) University of California at San Francisco, San Francisco, CA USA
SO Journal of Nuclear Medicine, (***May, 2000***) Vol. 41, No. 5 Suppl., pp. 312P. print.
Meeting Info.: 47th Annual Meeting of the Society of Nuclear Medicine St. Louis, Missouri, USA June 03-07, 2000 Society of Nuclear Medicine . ISSN: 0161-5505.
DT Conference
LA English
SL English

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(FILE 'HOME' ENTERED AT 18:58:33 ON 08 MAY 2002)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 18:58:42 ON 08 MAY 2002
L1 870 S WHOLE BODY IMAG?
L2 109 S L1 AND FLUOR?
L3 13 S L1 AND (GFP OR EGFP OR BFP OR RFP)
L4 7 DUP REM L3 (6 DUPLICATES REMOVED)
L5 1836 S WHOLE BODY (3A)IMAG?
L6 19 S L5 AND (GFP OR EGFP OR BFP OR RFP)
L7 10 DUP REM L6 (9 DUPLICATES REMOVED)
L8 8 S L1 AND LUCIFER?
L9 6 DUP REM L8 (2 DUPLICATES REMOVED)
L10 82 DUP REM L2 (27 DUPLICATES REMOVED)
L11 311 S L5 AND FLUOR?
L12 242 DUP REM L11 (69 DUPLICATES REMOVED)
L13 191 S L12 AND PY<=2000

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L14 7 L13 AND FLUORE?

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L15 7 DUP REM L14 (0 DUPLICATES REMOVED)

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In a multifile environment, a format can only be used if it is valid in at least one of the files. Refer to file specific help messages or the STNGUIDE file for information on formats available in individual files.
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REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):FIL BIOSIS MEDLINE EMBASE
'FIL' IS NOT A VALID FORMAT
'BIOSIS' IS NOT A VALID FORMAT
'MEDLINE' IS NOT A VALID FORMAT
'EMBASE' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid in at least one of the files. Refer to file specific help messages or the STNGUIDE file for information on formats available in individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):FIL STNGUIDE
'FIL' IS NOT A VALID FORMAT
'STNGUIDE' IS NOT A VALID FORMAT
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REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):filedefault

L15 ANSWER 1 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:12806 BIOSIS
DN PREV200100012806
TI Visualizing gene expression by ***whole*** - ***body*** ***fluorescence*** ***imaging*** .
AU Yang, Meng; Baranov, Eugene; Moossa, A. R.; Penman, Sheldon; Hoffman, Robert M. (1)
CS (1) AntiCancer, Inc., 7917 Ostrow Street, San Diego, CA, 92111: all@anticancer.com USA
SO Proceedings of the National Academy of Sciences of the United States of America, (***October 24, 2000***) Vol. 97, No. 22, pp. 12278-12282. print.
ISSN: 0027-8424.
DT Article
LA English
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(FILE 'HOME' ENTERED AT 18:58:33 ON 08 MAY 2002)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 18:58:42 ON 08 MAY 2002
L1 870 S WHOLE BODY IMAG?
L2 109 S L1 AND FLUOR?
L3 13 S L1 AND (GFP OR EGFP OR BFP OR RFP)
L4 7 DUP REM L3 (6 DUPLICATES REMOVED)
L5 1836 S WHOLE BODY (3A)IMAG?
L6 19 S L5 AND (GFP OR EGFP OR BFP OR RFP)
L7 10 DUP REM L6 (9 DUPLICATES REMOVED)
L8 8 S L1 AND LUCIFER?
L9 6 DUP REM L8 (2 DUPLICATES REMOVED)
L10 82 DUP REM L2 (27 DUPLICATES REMOVED)
L11 311 S L5 AND FLUOR?
L12 242 DUP REM L11 (69 DUPLICATES REMOVED)
L13 191 S L12 AND PY<=2000
L14 7 S L13 AND FLUORE?
L15 7 DUP REM L14 (0 DUPLICATES REMOVED)

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L15 ANSWER 1 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:12806 BIOSIS
DN PREV200100012806
TI Visualizing gene expression by ***whole*** - ***body*** ***fluorescence*** ***imaging*** .
AU Yang, Meng; Baranov, Eugene; Moossa, A. R.; Penman, Sheldon; Hoffman, Robert M. (1)
CS (1) AntiCancer, Inc., 7917 Ostrow Street, San Diego, CA, 92111: all@anticancer.com USA
SO Proceedings of the National Academy of Sciences of the United States of America, (***October 24, 2000***) Vol. 97, No. 22, pp. 12278-12282. print.
ISSN: 0027-8424.
DT Article
LA English
SL English
AB Transgene expression in intact animals now can be visualized by noninvasive techniques. However, the instruments and protocols developed so far have been formidable and expensive. We describe here a system for rapidly visualizing transgene expression in major organs of intact live mice that is simple, rapid, and eminently affordable. Green ***fluorescent*** protein (GFP) is expressed in the cells of brain, liver, pancreas, prostate, and bone, and its ***fluorescence*** is encoded in ***whole*** - ***body*** optical ***images*** . For low-magnification images, animals are illuminated atop a ***fluorescence*** light box and directly viewed with a thermoelectrically cooled color charge-coupled device camera. Higher-magnification images are made with the camera focused through an epi- ***fluorescence*** dissecting microscope. Both nude and normal mice were labeled by directly injecting 8 X 1010 plaque-forming units/ml of adenoviral GFP in 20-100 mul PBS and 10% glycerol into either the brain, liver, pancreas, prostate, or bone marrow. Within 5-8 h after adenoviral GFP injection, the ***fluorescence*** of the expressed GFP in brain and liver became visible, and ***whole*** - ***body*** ***images*** were recorded at video rates. The GFP ***fluorescence*** continued to increase for at least 12 h and remained detectable in liver for up to 4 months. The system's rapidity of image acquisition makes it capable of real-time recording. It requires neither exogenous contrast agents, radioactive substrates, nor long processing times. The method requires only that the expressed gene or promoter be fused or operatively linked to GFP. A comparatively modest investment allows the study of the therapeutic and diagnostic potential of suitably tagged genes in relatively opaque organisms.

L15 ANSWER 2 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:151951 BIOSIS
DN PREV200000151951
TI ***Whole*** - ***body*** optical ***imaging*** of green ***fluorescent*** protein-expressing tumors and metastases.
AU Yang, Meng; Baranov, Eugene; Jiang, Ping; Sun, Fang-Xian; Li, Xiao-Ming; Li, Lingna; Hasegawa, Satoshi; Bouvet, Michael; Al-Tuwaijri, Maraya; Chishima, Takashi; Shimada, Hiroshi; Moossa, A. R.; Penman, Sheldon; Hoffman, Robert M. (1)
CS (1) AntiCancer, Inc., 7917 Ostrow Street, San Diego, CA, 92111 USA
SO Proceedings of the National Academy of Sciences of the United States of America., (***Feb. 1, 2000***) Vol. 97, No. 3, pp. 1206-1211.
ISSN: 0027-8424.
DT Article
LA English
SL English
AB We have imaged, in real time, ***fluorescent*** tumors growing and metastasizing in live mice. The ***whole*** - ***body*** optical ***imaging*** system is external and noninvasive. It affords unprecedented continuous visual monitoring of malignant growth and spread within intact animals. We have established new human and rodent tumors that stably express very high levels of the Aequorea victoria green ***fluorescent*** protein (GFP) and transplanted these to appropriate animals. B16F0-GFP mouse melanoma cells were injected into the tail vein or portal vein of 6-week-old C57BL/6 and nude mice. ***Whole*** - ***body*** optical ***images*** showed metastatic lesions in the brain, liver, and bone of B16F0-GFP that were used for real time, quantitative measurement of tumor growth in each of these organs. The

AC3488-GFP human colon cancer was surgically implanted orthotopically into nude mice. ***Whole*** - ***body*** optical ***images*** showed, in real time, growth of the primary colon tumor and its metastatic lesions in the liver and skeleton. Imaging was with either a trans-illuminated epifluorescence microscope or a ***fluorescence*** light box and thermoelectrically cooled color charge-coupled device camera. The depth to which metastasis and micrometastasis could be imaged depended on their size. A 60-mum diameter tumor was detectable at a depth of 0.5 mm whereas a 1,800-mum tumor could be visualized at 2.2-mm depth. The simple, noninvasive, and highly selective imaging of growing tumors, made possible by strong GFP ***fluorescence*** , enables the detailed imaging of tumor growth and metastasis formation. This should facilitate studies of modulators of cancer growth including inhibition by potential chemotherapeutic agents.

L15 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:275343 BIOSIS
DN PREV200000275343
TI ***Whole*** - ***body*** optical ***imaging*** of green ***fluorescent*** protein-expressing tumors and metastases.
AU Yang, Meng (1); Baranov, Eugene; Jiang, Ping; Sun, Fang-Xian; Li, Xiao-Ming; Li, Lingna; Hasegawa, Satoshi; Bouvet, Michael; Chishima, Takashi; Shimada, Hiroshi; Moossa, A. R.; Hoffman, Robert M.
CS (1) AntiCancer Inc, San Diego, CA USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (***March, 2000***) No. 41, pp. 723. print..
Meeting Info.: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA April 01-05, 2000
ISSN: 0197-016X.
DT Conference
LA English
SL English

L15 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2002 ACS
AN 2000:516147 CAPLUS
DN 134:144026
TI External optical imaging of freely moving mice with green ***fluorescent*** protein-expressing metastatic tumors
AU Yang, Meng; Baranov, Eugene; Shimada, Hiroshi; Moossa, A. R.; Hoffman, Robert M.
CS AntiCancer, Inc., San Diego, CA, USA
SO Proceedings of SPIE-The International Society for Optical Engineering (***2000***), 3921(Optical Diagnostics of Living Cells III), 256-259
CODEN: PSISDG; ISSN: 0277-786X
PB SPIE-The International Society for Optical Engineering
DT Journal
LA English
AB We report here a new approach to genetically engineering tumors to become ***fluorescence*** such that they can be imaged externally in freely-moving animals. We describe here external high-resoln. real-time ***fluorescent*** optical imaging of metastatic tumors in live mice. Stable high-level green ***fluorescent*** protein (GFP)-expressing human and rodent cell lines enable tumors and metastasis is formed from them to be externally imaged from freely-moving mice. Real-time tumor and metastatic growth were quantitated from ***whole*** - ***body*** real-time ***imaging*** in GFP-expressing melanoma and colon carcinoma models. This GFP optical imaging system is highly appropriate for high throughput in vivo drug screening.
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:300206 BIOSIS
DN PREV200100300206
TI Visualizing leukemia & lymphoma cell homing and quantification of tumor burden in response to therapy in living animals.
AU Edinger, Matthias (1); Verneris, Michael R. (1); Cao, Yuan (1); Bachmann, Michael H. (1); Costa, Gina L. (1); Contag, Christopher H. (1); Negrin, Robert S. (1)
CS (1) Departments of Medicine and Pediatrics, Stanford University, School of Medicine, Stanford, CA USA
SO Blood, (***November 16, 2000***) Vol. 96, No. 11 Part 1, pp. 123a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DT Conference
LA English
SL English
AB Revealing the mechanisms of neoplastic disease and enhancing our ability to intervene in these processes requires an increased understanding of cellular and molecular changes as they occur in living animals. We have previously shown, that since light is transmitted through mammalian tissues at a low level, we can detect light emission from tumor cells that express luciferase from within living animals, using low light imaging cameras. To establish animal models of leukemia and lymphoma, we used the A20 and Bcl1 lymphoma cell lines. A20 cells were transfected with the pCDNA3.1-luc plasmid containing a modified luciferase gene (A20-luc). Using light emission as an indicator, tumor engraftment, exponential growth and rejection was followed in individual animals after sc, iv and ip injections. Tumor engraftment in spleen, liver and lymph nodes could be localized. As few as 103 A20-luc cells could be detected after sc injection. Following iv injection of 104 A20-luc cells in a syngeneic BMT model, leukemic disease was observed with tumor infiltration of the femurs, humeri, sternum, vertebrae and skull. A retroviral transduction system was used to transfer the gene for a GFP/luc fusion protein to the Bcl1 lymphoma, known to localize to liver and spleen. GFP expressing cells were sorted by FACS and injected into mice iv. Initially, as few as 7000 tumor cells could be detected, and subsequently tumor engraftment in liver and spleen was observed. Tumor growth was followed over time and quantified from these internal organs. We also investigated the therapeutic application of cytotoxic cells termed cytokine induced killer cells (CIK) which co-express T cell and NK cell markers and are generated by in vitro expansion from splenocytes. Treatment of A20-luc tumor bearing animals with 107 CIK cells led to a decrease of tumor signal from sc growing tumors and 75% of the mice were cured within 2 wks. To examine trafficking of these activated T cells we used the retroviral transduction method to label the cells. After iv injection transduced cells were detected in the lungs, 12 h later they locate to liver and spleen, and generalize thereafter. We conclude, that ***whole*** ***body*** ***imaging*** of labeled tumor cells reveals patterns of systemic disease allowing visualization of minimal disease and therapeutic response. This will improve our insights in tumor biology, be useful in directing subsequent ex vivo assays, and provide a powerful tool to examine the kinetics of response to novel therapies.

L15 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:231615 BIOSIS
DN PREV199900231615
TI In vivo imaging of tumors with protease-activated near-infrared ***fluorescent*** probes.
AU Weissleder, Ralph (1); Tung, Ching-Hsuan; Mahmood, Umar; Bogdanov, Alexei, Jr.
CS (1) Center of Molecular Imaging Research, Massachusetts General Hospital, Harvard Medical School, Boston, MA USA
SO Nature Biotechnology, (***April, 1999***) Vol. 17, No. 4, pp. 375-378.
ISSN: 1087-0156.
DT Article
LA English
SL English
AB We have developed a method to image tumor-associated lysosomal protease activity in a xenograft mouse model in vivo using autoquenched near-infrared ***fluorescence*** (NIRF) probes. NIRF probes were bound to a long circulating graft copolymer consisting of poly-L-lysine and methoxypolyethylene glycol succinate. Following intravenous injection, the NIRF probe carrier accumulated in solid tumors due to its long circulation time and leakage through tumor neovasculature. Intratumoral NIRF signal was generated by lysosomal proteases in tumor cells that cleave the macromolecule, thereby releasing previously quenched ***fluorochrome*** . In vivo imaging showed a 12-fold increase in NIRF signal, allowing the detection of tumors with submillimeter-sized diameters. This strategy can be used to detect such early stage tumors in vivo and to probe for specific enzyme activity.

L15 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1995:65925 BIOSIS
DN PREV199598080225
TI Migration of activated lymphocytes when adoptively transferred into cannulated rat brain.
AU Kruse, Carol A. (1); Kong, Qingzhong; Schiltz, Patric M.; Kleinschmidt-Demasters, Bette K.
CS (1) Dep. Pathol., Univ. Colorado Health Sci. Cent., Denver, CO 80262 USA
SO Journal of Neuroimmunology, (1994) Vol. 55, No. 1, pp. 11-21.
ISSN: 0165-5728.
DT Article
LA English
AB Migration of ***fluorescent*** DNA-labeled or 111Indium-labeled activated lymphocytes was studied in normal rat brain bearing surgically implanted cannulas. The migration of allogeneic cytotoxic T lymphocytes (CTL), derived from the DA rat (DA anti Fischer CTL), and of syngeneic concanavalin A (ConA)-activated lymphocytes (Fischer Con A blasts), was determined in Fischer rats between 2 h and 7 days post instillation into parietal brain. ***Whole*** ***body*** nuclear ***imaging*** indicated that the majority of the radiolabeled lymphocytes, either syngeneic or allogeneic, were present in the brain at 2 and at 18 h. Autoradiography of brain slices demonstrated that label was located throughout the brain and in both hemispheres at all time points. By direct tissue radioassay, approximately 60% of the injected dose was present between 2 and 18 h; this decreased to 18% by day 7. By ***fluorescence*** microscopy, large numbers of lymphocytes were visible up to 3-4 days. The lymphocytes traveled from the instillation site into both cerebral hemispheres primarily following white matter tracts. Preferential localization of ***fluorescently*** labeled lymphocytes was seen in the corpus callosum, internal and external capsules, anterior commissures, lateral olfactory tracts, white matter connections in the caudate and putamen, mammillothalamic and optic tracts. Overall, gray matter contained fewer cells although perivascular spaces within it had high concentrations of cells, indicating these spaces may act as points of egress.

=> s sugical orthotopic implantation or soi
L16 6383 SUGICAL ORTHOTOPIC IMPLANTATION OR SOI

=> d his

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FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 18:58:42 ON 08 MAY 2002
L1 870 S WHOLE BODY IMAG?
L2 109 S L1 AND FLUOR?
L3 13 S L1 AND (GFP OR EGFP OR BFP OR RFP)
L4 7 DUP REM L3 (6 DUPLICATES REMOVED)
L5 1836 S WHOLE BODY (3A)IMAG?
L6 19 S L5 AND (GFP OR EGFP OR BFP OR RFP)
L7 10 DUP REM L6 (9 DUPLICATES REMOVED)
L8 8 S L1 AND LUCIFER?
L9 6 DUP REM L8 (2 DUPLICATES REMOVED)
L10 82 DUP REM L2 (27 DUPLICATES REMOVED)
L11 311 S L5 AND FLUOR?
L12 242 DUP REM L11 (69 DUPLICATES REMOVED)
L13 191 S L12 AND PY<=2000
L14 7 S L13 AND FLUORE?
L15 7 DUP REM L14 (0 DUPLICATES REMOVED)
L16 6383 S SUGICAL ORTHOTOPIC IMPLANTATION OR SOI

=> s l5 and l16
L17 0 L5 AND L16

=> s l16 and py<2000
1 FILES SEARCHED...
L18 4542 L16 AND PY<2000

=> d bib abs 1-10

L18 ANSWER 1 OF 4542 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:17287 BIOSIS
DN PREV200100017287
TI Assessment of the predictability of seasonal rainfall in Ratnapura using the Southern Oscillation and its two extremes.
AU Punyawardena, B. V. R. (1); Cherry, N. J.
CS (1) Department of Agriculture, Natural Resources Management Centre, Peradeniya Sri Lanka
SO Journal of the National Science Foundation of Sri Lanka, (***September,*** *** 1999***) Vol. 27, No. 3, pp. 187-195. print.
ISSN: 1391-4588.
DT Article
LA English
SL English
AB An attempt is made to assess the predictability of seasonal rainfall at Ratnapura, namely, first intermonsoonal convectional rains (FIM), second intermonsoonal convectional rains (SIM), south-west monsoon rains (SWM) and north-east monsoon rains (NEM) by using Southern Oscillation and occurrence of El Nino and La Nina events. Seasonal rainfall data of Ratnapura and three monthly averaged Southern Oscillation Index (***SOI***) values for 118 consecutive years were analysed for lag correlation coefficients (CCs). The link between seasonal rainfall with El Nino or La Nina events was evaluated using binomial analysis. The association between FIM rains and the ***SOI*** shows a weak positive relationship. All the other seasonal rains, SWM, SIM and NEM are negatively related to the ***SOI*** . However, these relationships are weak and therefore cannot be used for any predictive purposes without wide margins of errors. The link of FIM rains (March to April) either with El Nino or La Nina events was not clear. Nevertheless, it is apparent that there is a strong tendency for above normal SIM rainfall (October to November) during El Nino years. If an El Nino year is immediately followed by a La Nifia year, both the FIM and SIM rains would produce above normal rains. It is interesting to note that the occurrence of "drought" conditions during the SWM season, May to September, is remote in a La Nina year. Significant associations between NEM rains (December to February) and El Nino or La Nina events were not observed.

L18 ANSWER 2 OF 4542 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:535674 BIOSIS
DN PREV200000535674
TI The nitrogen isotope biogeochemistry of sinking particles from the margin of the Eastern North Pacific.
AU Altabet, Mark A. (1); Pilskaln, Cynthia; Thunell, Robert; Pride, Carol; Sigman, Daniel; Chavez, Francisco; Francois, Roger
CS (1) Department of Chemistry and Biochemistry and Center for Marine Science and Technology, University of Massachusetts, Dartmouth, N. Dartmouth, MA, 02747 USA
SO Deep-Sea Research Part I Oceanographic Research Papers, (***April,*** *** 1999***) Vol. 46, No. 4, pp. 655-679. print.
ISSN: 0967-0637.
DT Article
LA English
SL English
AB The nitrogen isotopic composition of time-series sediment trap samples, dissolved NO3-, and surficial sediments was determined in three regions along the margin of the eastern North Pacific: Monterey Bay, San Pedro Basin, and the Gulf of California (Carmen and Guaymas Basins). Complex physical regimes are present in all three areas, and each is influenced seasonally by coastal upwelling. Nevertheless, sediment trap material evidently records the isotopic composition of new nitrogen sources, since average delta15N is generally indistinguishable from delta15N values for subsurface NO3-. Surficial sediments are also very similar to the average delta15N value of the sediment traps, being within 1permill. This difference in delta15N between trap material and sediment is much less than the previously observed 4permill difference for the deep sea. Better organic matter preservation at our margin sites is a likely explanation, which may be due to either low bottom O2 concentrations or higher organic matter input to the sediments. All sites have delta15N for sub-euphotic zone NO3- (8-10permill) substantially elevated from the oceanic average (4.5-5permill). This isotopic enrichment is a result of denitrification in suboxic subsurface waters (Gulf of California) or northward transport of denitrification influenced water (Monterey Bay and San Pedro Basin). Our results therefore suggest that downcore delta15N data, depending on site location, would record the intensity of denitrification and the transport of its isotopic signature along the California margin. Temporal variations in delta15N for the sediment traps do appear to respond to upwelling or convective injections of NO3- to surface waters as a result of isotopic fractionation during phytoplankton uptake. Overall, though, the coupling between NO3- injection, delta15N, and flux is looser than previously observed for the open-ocean, most likely the result of the smaller time/space scales of the events. In the Gulf of California, wintertime convective mixing/upwelling does produce distinct delta15N minima co-occurring with particle flux maxima. Interannual variations are apparent in this region when these wintertime delta15N minima fail to occur during El Nino conditions. There appears to be a positive relationship between the Southern Oscillation Index (***SOI***) anomaly and annual average delta15N. One explanation calls for hydrographic changes altering the delta15N of subeuphotic zone NO3-.

L18 ANSWER 3 OF 4542 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:248384 BIOSIS
DN PREV200000248384
TI Orthotopic metastatic mouse models for anticancer drug discovery and evaluation: A bridge to the clinic.
AU Hoffman, Robert M. (1)
CS (1) AntiCancer, Inc., 7917 Ostrow Street, San Diego, CA, 92111 USA
SO Investigational New Drugs, (1999) Vol. 17, No. 4, pp. 343-359.
ISSN: 0167-6997.
DT General Review
LA English
SL English
AB Currently used rodent tumor models, including transgenic tumor models, or subcutaneously-growing human tumors in immunodeficient mice, do not sufficiently represent clinical cancer, especially with regard to metastasis and drug sensitivity. In order to obtain clinically accurate models, we have developed the technique of surgical orthotopic implantation (***SOI***) to transplant histologically-intact fragments of human cancer, including tumors taken directly from the patient, to the corresponding organ of immunodeficient rodents. It has been demonstrated in 70 publications describing 10 tumor types that ***SOI*** allows the growth and metastatic potential of the transplanted tumors to be expressed and reflects clinical cancer. Unique clinically-accurate and relevant ***SOI*** models of human cancer for antitumor and antimetastatic drug discovery include: spontaneous ***SOI*** bone metastatic models of prostate cancer, breast cancer and lung cancer; spontaneous ***SOI*** liver and lymph node ultra-metastatic model of colon cancer, metastatic models of pancreatic, stomach, ovarian, bladder and kidney cancer. Comparison of the ***SOI*** models with transgenic mouse models of cancer indicate that the ***SOI*** models have more features of clinical metastatic cancer. Cancer cell lines have been stably transfected with the jellyfish Aequorea victoria green fluorescent protein (GFP) in order to track metastases in fresh tissue at ultra-high resolution and externally image metastases in the ***SOI*** models. Effective drugs can be discovered and evaluated in the ***SOI*** models utilizing human tumor cell lines and patient tumors. These unique ***SOI*** models have been used for innovative drug discovery and mechanism studies and serve as a bridge linking pre-clinical and clinical research and drug development.

L18 ANSWER 4 OF 4542 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:105305 BIOSIS
DN PREV200000105305
TI El Nino and decadal effects on sea-level variability in northern New Zealand: A wavelet analysis.
AU Goring, Derek G. (1); Bell, Robert G.
CS (1) National Institute of Water and Atmospheric Research Ltd, Christchurch New Zealand
SO New Zealand Journal of Marine and Freshwater Research, (***Dec., 1999***) Vol. 33, No. 4, pp. 587-598.
ISSN: 0028-8330.
DT Article
LA English
SL English
AB Sea-level data from two sites in northern New Zealand, along with the Southern Oscillation Index (***SOI***), are analysed for interannual and decadal variability using wavelets. The analysis shows, using

statistically significant wavelet power, there is a significant relationship between mean sea level (MSL) and ***SOI*** . However, the relationship is highly variable, both in magnitude and in the range of time-scales over which it occurs. This non-stationarity necessitates the use of techniques such as wavelets for analysis. An interdecadal response in MSL around northern New Zealand has been isolated, with shifts occurring in 1950 and the late 1970s. This behaviour in MSL appears to coincide with shifts in the Pacific Decadal Oscillation, thought previously to be largely centred in the North Pacific. A strong correlation between ***SOI*** and sea surface temperature (SST) is also demonstrated. This relationship appears to be stable in magnitude (a large change in ***SOI*** produces a large change in SST) and to occur over the same range of time-scales. More SST and MSL data are required for other parts of New Zealand to determine whether these findings apply elsewhere.

L18 ANSWER 5 OF 4542 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:102743 BIOSIS
DN PREV200000102743
TI Feeding kinematics of Phelsuma madagascariensis (Reptilia: Gekkonidae): Testing differences between Iguania and Scleroglossa.
AU Delheusy, Veronique; Bels, Vincent L. (1)
CS (1) Centre Agronomique de Recherches Appliquees du Hainaut, rue de l'Agriculture 301, B-7800, Ath Belgium
SO Journal of Experimental Biology, (***Dec., 1999***) Vol. 202, No. 24, pp. 3715-3730.
ISSN: 0022-0949.
DT Article
LA English
SL English
AB The kinematics of feeding in the gekkotan lizard Phelsuma madagascariensis (Scleroglossa) was investigated using high-speed cinematography (200-300 frames s-1) and X-ray films (64 frames s-1). Qualitative kinematic analysis of the head and jaw displacement of the prey to (capture) and within (reduction, transport, swallowing, licking) the buccal cavity are compared for two types of prey (crickets and mealworms) in 30 feeding sequences from four individuals. Maximal displacement of structures and timing of events are compared statistically to assess the differences among the phases and the prey using analysis of variance. P. madagascariensis uses its jaws only to capture the two types of prey item, and the capture jaw cycle is divided into fast-opening (FO), fast-closing (FC) and slow-closing (SC) stages only. As in iguanians and other scleroglossans, the reduction and transport cycles always involve a slow opening (***SOI*** and SOII) stage before the FO stage, followed by FC and SC stages: this last stage was not easily identified in all feeding phase. Transport of the prey was followed by a large number of licking cycles. Our data show (i) that the capture profile in gekkotans is similar to that observed for other scleroglossans and different from that described for iguanians (e.g. the absence of an SO stage); (ii) that the kinematics of jaw and related hyo-lingual cycles of intraoral manipulation (reduction and transport) are similar in lizards with a very different hyo-lingual system (Iguania, Gekkota and Scincomorpha), suggesting a basic mechanism of feeding cycles in squamates, transformed in varanids and snakes; and (iii) that prey type affects the kinematics of capture and manipulation, although the high level of variation among lizards suggests a possible individual modulation of feeding mechanism. A principal components analysis was performed to compare capture and transport cycles in this study of P. madagascariensis (Gekkota) and a previous study of Oplurus cuvieri (Iguania). This analysis separated the capture cycle of each species, but the transport cycles were not completely separated. These results demonstrate the complexity of the modulation and evolution of feeding process in squamates.

L18 ANSWER 6 OF 4542 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:76490 BIOSIS
DN PREV200000076490
TI Southern oscillation and the northern Australian prawn catch.
AU Catchpole, A. (1); Auliciems, A.
CS (1) Institute of Antarctic and Southern Ocean Studies, University of Tasmania, Sandy Bay, TAS, 7005 Australia
SO International Journal of Biometeorology, (***Nov., 1999***) Vol. 43, No. 3, pp. 110-112.
ISSN: 0020-7128.
DT Article
LA English
SL English
AB Associations are established between the southern oscillation index (***SOI***) and penaeid prawn catches within the northern Australian prawn fishery. Analysis involved calculation of correlations between Gulf of Carpentaria banana prawn and tiger prawn catches and Troup's ***SOI*** . Significant positive correlations are observed between catch size and ***SOI*** for specific months from pre-wet to post-wet seasons. For banana prawns, the results indirectly confirm some earlier observations of increased catches in conjunction with high rainfall during the onset of monsoon periods, but also indicate an association with late rains. However, the relationship with tiger prawns appears to be in the opposite direction, showing negative correlations with ***SOI*** for particular months. Some hypotheses are suggested to explain these results in terms of environmental effects on spawning populations, and comment is made on the potential for forecasting catch sizes.

L18 ANSWER 7 OF 4542 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:59827 BIOSIS
DN PREV200000059827
TI Improved metastatic animal model of human prostate carcinoma using surgical orthotopic implantation (***SOI*** .
AU Chang, X. H.; Fu, Y. W.; Na, W. L.; Wang, J.; Sun, H.; Cai, L. (1)
CS (1) Department of Pathology, The University of Western Ontario, London, Ontario Canada
SO Anticancer Research, (***Sept. Oct., 1999***) Vol. 19, No. 5B, pp. 4199-4202.
ISSN: 0250-7005.
DT Article
LA English
SL English
AB Background. An animal model demonstrating high metastasis of human prostate carcinoma is of importance in studying the biology and therapy of human prostate carcinoma Dr. Hoffman's group recently used surgical orthotopic implantation (***SOI***) of human prostate cells to nude mice to establish an animal model with high metastatic activity. To confirm the animal model by ***SOI*** reproducible in other laboratories and shorten the period requiring for the metastasis, we adopted ***SOI*** technique with a modification using PC-3M human prostate cell line which showed a higher metastatic activity than PC-3. Materials and Methods. Intact tissue of the human prostate carcinoma cell line PC-3M was prepared by growth of this cell subcutaneous in a nude mouse. One piece of 1.5 mm3 intact tumor tissue was implanted by orthotopical surgery to the ventral lateral lobes of the prostate gland of 10 nude mice. Mice were sacrificed when they were found to be moribund. Metastasis in other tissues was evaluated by gross and microscopic morphology. Results: All 10 mice showed the tumorigenesis in the prostate gland and metastasis of human prostate tumor cells into periaortic lymph nodes without other organ's metastasis. The time when mice with PC-3M ***SOI*** start moribund is 28 - 32 days after ***SOI*** . Conclusions: ***SOI*** is good technique to establish the efficiently metastatic animal mode. ***SOI*** using PC-3M human prostate cell line will leads to 100% metastasis of prostate tumor cells. So far, this model is much quicker and more efficient than those reported in literatures.

L18 ANSWER 8 OF 4542 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:52184 BIOSIS
DN PREV200000052184
TI Incidence of plague associated with increased winter-spring precipitation in New Mexico.
AU Parmenter, Robert R. (1); Yadav, Ekta Pratap; Parmenter, Cheryl A.; Ettestad, Paul; Gage, Kenneth L.
CS (1) Department of Biology, University of New Mexico, 167 Castetter Hall, Albuquerque, NM USA
SO American Journal of Tropical Medicine and Hygiene, (***Nov., 1999***) Vol. 61, No. 5, pp. 814-821.
ISSN: 0002-9637.
DT Article
LA English
SL English
AB Plague occurs episodically in many parts of the world, and some outbreaks appear to be related to increased abundance of rodents and other mammals that serve as hosts for vector fleas. Climate dynamics may influence the abundance of both fleas and mammals, thereby having an indirect effect on human plague incidence. An understanding of the relationship between climate and plague could be useful in predicting periods of increased risk of plague transmission. In this study, we used correlation analyses of 215 human cases of plague in relation to precipitation records from 1948 to 1996 in areas of New Mexico with history of human plague cases (38 cities, towns, and villages). We conducted analyses using 3 spatial scales: global (El Nino-Southern Oscillation Indices (***SOI***)); regional (pooled state-wide precipitation averages); and local (precipitation data from weather stations near plague case sites). We found that human plague cases in New Mexico occurred more frequently following winter-spring periods (October to May) with above-average precipitation (mean plague years = 113% of normal rain/snowfall), resulting in 60% more cases of plague in humans following wet versus dry winter-spring periods. However, we obtained significant results at local level only; regional state-wide precipitation averages and ***SOI*** values exhibited no significant correlations to incidence of human plague cases. These results are consistent with our hypothesis of a trophic cascade in which increased winter-spring precipitation enhances small mammal food resource productivity (plants and insects), leading to an increase in the abundance of plague hosts. In addition, moister climate conditions may act to promote flea survival and reproduction, also enhancing plague transmission. Finally, the result that the number of human plague cases in New Mexico was positively associated with higher than normal winter-spring precipitation at a local scale can be used by physicians and public health personnel to identify and predict periods of increased risk of plague transmission to humans.

L18 ANSWER 9 OF 4542 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:16150 BIOSIS
DN PREV200000016150
TI Tree-shrub interactions in a subtropical savanna parkland: Competition or facilitation.
AU Barnes, Paul W. (1); Archer, Steve

CS (1) Department of Biology, Southwest Texas State University, San Marcos, TX, 78666-4616 USA
SO Journal of Vegetation Science, (***Aug., 1999***) Vol. 10, No. 4, pp. 525-536.
ISSN: 1100-9233.
DT Article
LA English
SL English
AB Prosopis glandulosa var. glandulosa has played a central role in the encroachment of woody plants in southern Texas, grasslands and savannas by acting as a nurse plant for various shrubs that establish in its understory. To test for continued facilitation of established understory shrubs by Prosopis and to determine if established shrubs compete with the Prosopis nucleus, selective removal experiments were conducted and monitored over a 2 - 5 yr period. Short-term (1 - 3 days) and long-term (2 yr) growth and physiological activities (midday net photosynthesis and leaf/shoot water potential) of two common understory shrubs, Zanthoxylum fagara and Berberis trifoliolata, growing with Prosopis, were generally comparable to those of individuals occurring in clusters where Prosopis was removed. Shrubs growing with an intact Prosopis occasionally showed significantly higher leaf-(N) and pre-dawn water potentials than those in clusters lacking a live Prosopis, especially under d rought conditions; however, these differences did not translate into greater midday leaf gas exchange or shoot growth. By comparison, removal of understory shrubs elicited large increases in Prosopis net photosynthesis, annual trunk growth in each of the 5 yr monitored, and seed pod production in three of the four years monitored. Seven of 26 Prosopis plants in experimental clusters with an intact understory died over a 5-yr period, compared to only two of the 26 plants in clusters with the cleared understory. Results indicate that (1) the founding overstory Prosopis plant may continue to facilitate understory shrubs following their establishment, but these beneficial effects appear to be small and transitory, and (2) the understory shrubs have a pronounced negative effect on Prosopis, such that competition between overstory and understory woody plants is strongly asymmetrical. These findings suggest that understory shrubs will likely persist despite changes in microclimate and ***soi*** ls (potentially) that occur after the Prosopis plant, which facilitated their ingress or establishment, has died. Soil resource depletion by shallow-rooted understory shrubs appears to be a primary factor contributing to the demise of the deeply rooted, overstory Prosopis plants, especially on upland sites with duplex soils where below-ground competition is accentuated.

L18 ANSWER 10 OF 4542 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:16108 BIOSIS
DN PREV200000016108
TI Persistent seed banks: Delayed seed germination models and their application to alpine environments.
AU Cavieres, Lohengrin A. (1)
CS (1) Departamento de Botanica, Facultad de Ciencias Naturales y Oceanograficas, Universidad de Concepcion, Concepcion Chile
SO Revista Chilena de Historia Natural, (***Sept., 1999***) Vol. 72, No. 3, pp. 457-466.
ISSN: 0716-078X.
DT Article
LA Spanish
SL English; Spanish
AB Seed banks are ecological and evolutionary important for many plant species. Seed banks are classified as transient if seeds germinate in the same year when they are produced, or persistent if a proportion of seeds germinates during the year of production, with some seeds remaining viable at least one year after. Due to harshness of climate, in arctic and alpine environments vegetative reproduction would be more advantageous than sexual reproduction. Moreover, considering the high longevity of species inhabiting this zone, the maintenance of seeds in the soil would not be necessary. However, numerous studies have reported the presence of soil seed banks in many arctic and alpine sites. Most of these works are descriptions on the composition and magnitude of the seed bank, with no distinction between transient and persistent components. Also, in these studies there is no discussion whether seed bank is a reflection of an accumulation of seeds whose persistence is favored by the good ***soi*** l conditions to maintain viable seeds, or a life history trait that has been selected in alpine environments. Here I review three theoretical models that predict conditions for the evolution of seed dormancy and discuss their application to alpine zones. According to the analyses, the presence of seed dormancy and formation of persistent seed banks could be expected in alpine plant communities as a life history trait selected in those environments. Experimental evidences indicate that alpine species have the seed dormancy mechanisms that enable them to form highly longeve persistent seed bank.

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L1 870 S WHOLE BODY IMAG?
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L3 13 S L1 AND (GFP OR EGFP OR BFP OR RFP)
L4 7 DUP REM L3 (6 DUPLICATES REMOVED)
L5 1836 S WHOLE BODY (3A)IMAG?
L6 19 S L5 AND (GFP OR EGFP OR BFP OR RFP)
L7 10 DUP REM L6 (9 DUPLICATES REMOVED)
L8 8 S L1 AND LUCIFER?
L9 6 DUP REM L8 (2 DUPLICATES REMOVED)
L10 82 DUP REM L2 (27 DUPLICATES REMOVED)
L11 311 S L5 AND FLUOR?
L12 242 DUP REM L11 (69 DUPLICATES REMOVED)
L13 191 S L12 AND PY<=2000
L14 7 S L13 AND FLUORE?
L15 7 DUP REM L14 (0 DUPLICATES REMOVED)
L16 6383 S SUGICAL ORTHOTOPIC IMPLANTATION OR SOI
L17 0 S L5 AND L16
L18 4542 S L16 AND PY<2000

=> s sugical orthotopic implantation
L19 0 SUGICAL ORTHOTOPIC IMPLANTATION

=> s surgical orthotopic implantation
L20 83 SURGICAL ORTHOTOPIC IMPLANTATION

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L21 0 L20 AND L5

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=> s l22 and py<2000
1 FILES SEARCHED...
L23 32 L22 AND PY<2000

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L23 ANSWER 1 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:248384 BIOSIS
DN PREV200000248384
TI Orthotopic metastatic mouse models for anticancer drug discovery and evaluation: A bridge to the clinic.
AU Hoffman, Robert M. (1)
CS (1) AntiCancer, Inc., 7917 Ostrow Street, San Diego, CA, 92111 USA
SO Investigational New Drugs, (1999) Vol. 17, No. 4, pp. 343-359.
ISSN: 0167-6997.
DT General Review
LA English
SL English
AB Currently used rodent tumor models, including transgenic tumor models, or subcutaneously-growing human tumors in immunodeficient mice, do not sufficiently represent clinical cancer, especially with regard to metastasis and drug sensitivity. In order to obtain clinically accurate models, we have developed the technique of ***surgical*** ***orthotopic*** ***implantation*** (SOI) to transplant histologically-intact fragments of human cancer, including tumors taken directly from the patient, to the corresponding organ of immunodeficient rodents. It has been demonstrated in 70 publications describing 10 tumor types that SOI allows the growth and metastatic potential of the transplanted tumors to be expressed and reflects clinical cancer. Unique clinically-accurate and relevant SOI models of human cancer for antitumor and antimetastatic drug discovery include: spontaneous SOI bone metastatic models of prostate cancer, breast cancer and lung cancer; spontaneous SOI liver and lymph node ultra-metastatic model of colon cancer, metastatic models of pancreatic, stomach, ovarian, bladder and kidney cancer. Comparison of the SOI models with transgenic mouse models of cancer indicate that the SOI models have more features of clinical metastatic cancer. Cancer cell lines have been stably transfected with the jellyfish Aequorea victoria green fluorescent protein (GFP) in order to track metastases in fresh tissue at ultra-high resolution and externally image metastases in the SOI models. Effective drugs can be discovered and evaluated in the SOI models utilizing human tumor cell lines and patient tumors. These unique SOI models have been used for innovative drug discovery and mechanism studies and serve as a bridge linking pre-clinical and clinical research and drug development.

L23 ANSWER 2 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:59827 BIOSIS
DN PREV200000059827
TI Improved metastatic animal model of human prostate carcinoma using ***surgical*** ***orthotopic*** ***implantation*** (SOI.
AU Chang, X. H.; Fu, Y. W.; Na, W. L.; Wang, J.; Sun, H.; Cai, L. (1)
CS (1) Department of Pathology, The University of Western Ontario, London, Ontario Canada
SO Anticancer Research, (***Sept. Oct., 1999***) Vol. 19, No. 5B, pp. 4199-4202.

ISSN: 0250-7005.
DT Article
LA English
SL English
AB Background. An animal model demonstrating high metastasis of human prostate carcinoma is of importance in studying the biology and therapy of human prostate carcinoma Dr. Hoffman's group recently used ***surgical*** ***orthotopic*** ***implantation*** (SOI) of human prostate cells to nude mice to establish an animal model with high metastatic activity. To confirm the animal model by SOI reproducible in other laboratories and shorten the period requiring for the metastasis, we adopted SOI technique with a modification using PC-3M human prostate cell line which showed a higher metastatic activity than PC-3. Materials and Methods. Intact tissue of the human prostate carcinoma cell line PC-3M was prepared by growth of this cell subcutaneous in a nude mouse. One piece of 1.5 mm3 intact tumor tissue was implanted by orthotopical surgery to the ventral lateral lobes of the prostate gland of 10 nude mice. Mice were sacrificed when they were found to be moribund. Metastasis in other tissues was evaluated by gross and microscopic morphology. Results: All 10 mice showed the tumorigenesis in the prostate gland and metastasis of human prostate tumor cells into periaortic lymph nodes without other organ's metastasis. The time when mice with PC-3M SOI start moribund is 28 - 32 days after SOI. Conclusions: SOI is good technique to establish the efficiently metastatic animal mode. SOI using PC-3M human prostate cell line will leads to 100% metastasis of prostate tumor cells. So far, this model is much quicker and more efficient than those reported in literatures.

L23 ANSWER 3 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:428633 BIOSIS
DN PREV199900428633
TI Development of a high metastatic orthotopic model of human renal cell carcinoma in nude mice: Benefits of fragment implantation compared to cell-suspension injection.
AU An, Zili; Jiang, Ping; Wang, Xiaoen; Moossa, A. R.; Hoffman, Robert M. (1)
CS (1) AntiCancer, Inc., 7917 Ostrow St., San Diego, CA, 92111 USA
SO Clinical & Experimental Metastasis, (***May, 1999***) Vol. 17, No. 3, pp. 265-270.
ISSN: 0262-0898.
DT Article
LA English
SL English
AB In this study we compared the metastatic rate of human renal cell carcinoma SN12C in two orthotopic nude mouse models: ***surgical*** ***orthotopic*** ***implantation*** (SOI) of histologically intact tumor tissue and cellular orthotopic injection (COI) of cell suspensions in the kidney. The primary tumors resulting from SOI were larger and much more locally invasive than primary tumors resulting from COI. SOI generated higher metastatic expression than COI. The differences in metastatic rates in the involved organs (lung, liver, and mediastinal lymph nodes) were 2-3 fold higher in SOI compared to COI ($P < 0.05$). Median survival time in the SOI model was 40 days, which was significantly shorter than that of COI (68 days) ($P < 0.001$). Histological observation of the primary tumors from the SOI model demonstrated a much richer vascular network than the COI model. Lymph node and lung metastases were larger and more cellular in the SOI model compared to COI. We conclude that the tissue architecture of the implanted tumor tissue in the SOI model plays an important role in the initiation of primary tumor growth, invasion, and distant metastasis. This study directly demonstrates that the implantation of histologically intact tumor tissue orthotopically allows accurate expression of the clinical features of human renal cancer in nude mice. This model should be of value in cancer research and antimetastatic drug discovery for renal cancer, a currently very poorly responding malignancy.

L23 ANSWER 4 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:366080 BIOSIS
DN PREV199900366080
TI An ultra-metastatic model of human colon cancer in nude mice.
AU Sun, Fang X.; Sasson, Aaron R.; Jiang, Ping; An, Zili; Gamagami, Reza; Li, Lingna; Moossa, A. R.; Hoffman, Robert M. (1)
CS (1) AntiCancer, Inc., 7917 Ostrow Street, San Diego, CA, 92111 USA
SO Clinical & Experimental Metastasis, (***Feb., 1999***) Vol. 17, No. 1, pp. 41-48.
ISSN: 0262-0898.
DT Article
LA English
SL English
AB An ultra-high metastatic model of human colon cancer was developed in order to represent highly malignant patient disease for which there is no current model. ***Surgical*** ***orthotopic*** ***implantation*** (SOI) of a histologically intact liver metastasis fragment derived from a surgical specimen of a patient with metastatic colon cancer was initially implanted in the colon, liver and subcutaneously in nude mice. This tumor did not metastasize for the first 10 passages. At the eleventh passage, the tumor exhibited metastasis from the colon to the liver, spleen, and lymph nodes. At this time, two selective passages were carried out by transplanting resulting liver metastases in the nude mice to the colon of additional nude mice. After these two passages, the tumor became stably ultra-metastatic and was termed AC3488UM. One-hundred percent of mice transplanted with AC3488UM with SOI to the colon exhibited local growth, regional invasion, and spontaneous metastasis to the liver, lymph nodes, and spleen. While the maximum size of the primary tumor was 0.9 g, the metastatic liver was over 9 times the weight of the normal liver with the maximum weight of the metastatic liver over 12 g. Liver metastases were detected by the tenth day after transplantation in all animals. Half the animals died of metastatic tumor 25 days after transplantation. Histological characteristics of AC3488UM tumor were poorly differentiated adenocarcinoma of colon. Mutant p53 is expressed heterogeneously in the primary tumor and more homogeneously in the liver metastasis suggesting a possible role of p53 in the liver metastasis. The human origin of AC3488UM was confirmed by positive fluorescence staining for in situ hybridization of human DNA. The AC3488 human colon-tumor model with its ultra-high metastatic capability in each transplanted animal, short latency and a short median survival period is different from any known human colon cancer model and will be an important tool for the study of and development ofnew therapy for highly metastatic human colon cancer.

L23 ANSWER 5 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:261886 BIOSIS
DN PREV199900261886
TI High-malignancy orthotopic nude mouse model of human prostate cancer LNCaP.
AU Wang, Xiaoen; An, Zili; Geller, Jack; Hoffman, Robert M. (1)
CS (1) AntiCancer, Inc., 7917 Ostrow St., San Diego, CA, 92111 USA
SO Prostate, (***May 15, 1999***) Vol. 39, No. 3, pp. 182-186.
ISSN: 0270-4137.
DT Article
LA English
SL English
AB BACKGROUND. An animal model of human prostate cancer LNCaP demonstrating high rates of spontaneous metastasis from the orthotopic site after tumor implantation would be very valuable for mechanistic and drug discovery studies. We previously developed microsurgical techniques to implant histologically intact tumor tissues orthotopically in nude mice in order to develop high metastatic mouse models of human cancer. METHODS. Intact tissue of the androgen-dependent human prostate cancer cell line, LNCaP, was implanted on the ventral lateral lobes of the prostate gland by ***surgical*** ***orthotopic*** ***implantation*** (SOI) in a series of 20 nude mice. Mice were autopsied, and histopathological examination of primary tumors and relevant organs was done to identify and quantitate micrometastasis. RESULTS. Eighteen of 20 animals transplanted with LNCaP by SOI had tumor growth. Mean primary tumor weight in the prostate was 9.24 g at time of necropsy. Sixty-one percent of the transplanted animals had lymph node metastasis. Forty-four percent had lung metastasis. Mean survival time was 72 days, indicating a high degree of malignancy of the tumor. CONCLUSIONS. The extensive and widespread lung metastasis as well as lymph node metastasis following orthotopic implantation of LNCaP in nude mice and the short survival time provide a high-malignancy nude model of the LNCaP human prostate tumor.

L23 ANSWER 6 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:259370 BIOSIS
DN PREV199900259370
TI Cimetidine: An inhibitor or promoter of tumor growth.
AU Sasson, A. R. (1); Gamagami, R. (1); An, Z. (1); Wang, X. (1); Moossa, A. R. (1); Hoffman, R. M. (1)
CS (1) AntiCancer, Inc., 7917 Ostrow Street, San Diego, CA, 92111 USA
SO International Journal of Cancer, (***May 31, 1999***) Vol. 81, No. 5, pp. 835-838.
ISSN: 0020-7136.
DT Letter; Article
LA English

L23 ANSWER 7 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:244923 BIOSIS
DN PREV199900244923
TI Efficacy of new platinum analog DPPE in an orthotopic nude mouse model of human colon cancer.
AU Rho, Young-Soo; Lee, Kyung-Tae; Jung, Jee-Chang; Yoon, Choong; An, Zili; Hoffman, Robert M.; Chang, Sung-Goo (1)
CS (1) Department of Urology, Kyung Hee University Medical Center, No. 1 Hoegidong Dongdaemunku, Seoul, 130-702 South Korea
SO Anticancer Research, (***Jan.-Feb., 1999***) Vol. 19, No. 1A, pp. 157-162.
ISSN: 0250-7005.
DT Article
LA English
SL English
AB A ***surgical*** ***orthotopic*** ***implantation*** (S.O.I.) model of the human colon cancer cell line Co-3 in nude mice was treated with two doses of the new platinum analogs (Pt(cis-dach) (DPPE)cntdot2NO3) and (Pt(trans-dach)(DPPE)cntdot2NO3). The analogs were evaluated for antimetastatic efficacy in comparison to two doses of cisplatinum. Unlike the untreated control group, there were no mesenteric lymph node metastases in the groups treated with the high or low doses of both forms of new DPPE platinum analogs as well as cisplatinum-treated group. However, much more body-weight loss occurred in the cisplatinum-treated

group than the DPPE-treated groups. The results obtained with SOI animal model of colon cancer demonstrated both cis- and trans-forms of DPPE had as strong an inhibitory effect on metastasis as that of cisplatinum, but with much less toxicity. Thus the new platinum analogs appears to have promising clinical potential.

L23 ANSWER 8 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:234768 BIOSIS
DN PREV199900234768
TI Fertile seed and rich soil: The development of patient-like models of metastatic human cancer by ***surgical*** ***orthotopic*** ***implantation*** of intact tissue.
AU Hoffman, Robert M. (1)
CS (1) Lab. Cancer Biol., Sch. Med., Univ. Calif., San Diego USA
SO Yokohama Medical Bulletin, (1995) Vol. 46, No. 3-4, pp. 71.
Meeting Info.: Eighth Yokohama City University International Academic Symposium on Basic and Clinical Studies on Cancer Metastasis Yokohama City, Japan October 6-7, 1995 Yokohama City University
. ISSN: 0044-0531.
DT Conference
LA English

L23 ANSWER 9 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:192891 BIOSIS
DN PREV199900192891
TI Survival efficacy of the combination of the methioninase gene and methioninase gene product in a human lung cancer orthotopic model.
AU Miki, K. (1); Xu, M. (1); An, Z. (1); Wang, X. (1); Yang, M. (1); Zhao, M. (1); Sun, X. (1); Tan, Y. (1); Moossa, A. R.; Hoffman, R. M. (1)
CS (1) AntiCancer Inc., San Diego, CA USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (***March, 1999***) Vol. 40, pp. 598.
Meeting Info.: 90th Annual Meeting of the American Association for Cancer Research Philadelphia, Pennsylvania, USA April 10-14, 1999 American Association for Cancer Research
. ISSN: 0197-016X.
DT Conference
LA English

L23 ANSWER 10 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:192691 BIOSIS
DN PREV199900192691
TI A fluorescent orthotopic bone metastasis model of human prostate cancer.
AU Yang, M. (1); Jiang, P. (1); Sun, F. X. (1); An, Z. (1); Hasegawa, S. (1); Chishima, T.; Shimada, H.; Moossa, A. R.; Hoffman, R. M. (1)
CS (1) AntiCancer Inc., San Diego, CA USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (***March, 1999***) Vol. 40, pp. 328.
Meeting Info.: 90th Annual Meeting of the American Association for Cancer Research Philadelphia, Pennsylvania, USA April 10-14, 1999 American Association for Cancer Research
. ISSN: 0197-016X.
DT Conference
LA English

L23 ANSWER 11 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:143881 BIOSIS
DN PREV199900143881
TI A fluorescent orthotopic bone metastasis model of human prostate cancer.
AU Yang, Meng; Jiang, Ping; Fang-Xian; Hasegawa, Satoshi; Baranov, Eugene; Chishima, Takashi; Shimada, Hiroshi; Moossa, A. R.; Hoffman, Robert M. (1)
CS (1) AntiCancer Inc., 7917 Ostrow St., San Diego, CA 92111 USA
SO Cancer Research, (***Feb. 15, 1999***) Vol. 59, No. 4, pp. 781-786.
ISSN: 0008-5472.
DT Article
LA English
AB Here, we report a fluorescent spontaneous bone metastatic model of human prostate cancer developed by ***surgical*** ***orthotopic*** ***implantation*** of green fluorescent protein (GFP)-expressing prostate cancer tissue. Human prostate cancer PC-3 cells were transduced with the pLEIN expression retroviral vector containing the enhanced GFP and neomycin resistance genes. Stable GFP high-expression PC-3 clones were selected in vitro with G418, which were then combined and injected s.c. in nude mice. For metastasis studies, fragments of a single highly fluorescent s.c. growing tumor were implanted by ***surgical*** ***orthotopic*** ***implantation*** in the prostate of a series of nude mice. Subsequent micrometastases and metastases were visualized by GFP fluorescence throughout the skeleton, including the skull, rib, pelvis, femur, and tibia. The central nervous system, including the brain and spinal cord, was also involved with tumor, as visualized by GFP fluorescence. Systemic organs, including the lung, plural membrane, liver, kidney, and adrenal gland, also had fluorescent metastases. The metastasis pattern in this model reflects the bone and other metastatic sites of human prostate cancer. Thus, this model should be very useful for the study and development of treatment for metastatic androgen-independent prostate cancer.

L23 ANSWER 12 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:482102 BIOSIS
DN PREV199800482102
TI Widespread skeletal metastatic potential of human lung cancer revealed by green fluorescent protein expression.
AU Yang, Meng; Hasegawa, Satoshi; Jiang, Ping; Wang, Xiaoen; Tan, Yuying; Chishima, Takashi; Shimada, Hiroshi; Moossa, A. R.; Hoffman, Robert M. (1)
CS (1) AntiCancer Inc., San Diego, CA 92111 USA
SO Cancer Research, (***Oct. 1, 1998***) Vol. 58, No. 19, pp. 4217-4221.
ISSN: 0008-5472.
DT Article
LA English
AB To understand the skeletal metastatic pattern of non-small cell lung cancer, we developed a stable high-expression gm fluorescent protein (GFP) transductant of human lung cancer cell line H460 (H460-GFP). The GFP-expressing lung cancer was visualized to metastasize widely throughout the skeleton when implanted orthotopically in nude mice. H460 was transduced with the pLEIN retroviral expression vector containing the enhanced GFP and the neomycin (G418) resistance gene. A stable high GFP-expressing clone was selected in vitro using 800 mug/ml G418. Stable high-level expression of GFP was maintained in s.c.-growing tumors formed after injecting H460-GFP cells in nude mice. To use H460-GFP for visualization of metastasis, fragments of s.c.-growing H460-GFP tumors were implanted by ***surgical*** ***orthotopic*** ***implantation*** in the left lung of nude mice. Subsequent micrometastases were visualized by GFP fluorescence in the contralateral lung, plural membrane, and widely throughout the skeletal system including the skull, vertebra, femur, tibia, pelvis, and bone marrow of the femur and tibia. The use of GFP-expressing H460 cells transplanted by ***surgical*** ***orthotopic*** ***implantation*** revealed the extensive metastatic potential of lung cancer in particular to widely disseminated sites throughout the skeleton. This new metastatic model can play a critical role in the study of the mechanism of skeletal and other metastasis in lung cancer and in screening of therapeutics that prevent or reverse this process.

L23 ANSWER 13 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:168441 BIOSIS
DN PREV199800168441
TI ***Surgical*** ***orthotopic*** ***implantation*** allows high lung and lymph node metastatic expression of human prostate carcinoma cell line PC-3 in nude mice.
AU An, Zili; Wang, Xiaoen; Geller, Jack (1); Moossa, A. R.; Hoffman, Robert M.
CS (1) AntiCancer Inc., 7917 Ostrow St., San Diego, CA 92111 USA
SO Prostate, (***Feb. 15, 1998***) Vol. 34, No. 3, pp. 169-174.
ISSN: 0270-4137.
DT Article
LA English
AB BACKGROUND. Prostate cancer is the second leading cause of male death in the United States. When diagnosed, nearly half the cases have metastatic lesions. An animal model of human prostate cancer demonstrating spontaneous metastasis from the orthotopic site after tumor implantation should be of great help for us to understand the disease and to formulate treatment strategy. We report here a high metastatic model of human prostate cancer PC-3. METHODS. We developed microsurgical techniques, termed ***surgical*** ***orthotopic*** ***implantation*** (SOI), to implant histologically intact tumor tissues orthotopically in immunodeficient mice. In this study intact tissue of the human prostate cancer cell line PC-3, harvested from a subcutaneous tumor in a nude mouse, was implanted to the ventral lateral lobes of the prostate gland in a series of nude mice. Mice were sacrificed when found moribund, and autopsy and histology were performed subsequently. RESULTS. A high frequency of lymph node and lung metastasis was noted upon histological examination. The extensive and widespread lung metastasis following orthotopic implantation of PC-3 is, to the best of our knowledge, the first report in the literature. CONCLUSIONS. In contrast to orthotopic injection of cell suspensions, no multiple metastatic cell selection was necessary after SOI for significant expression of the metastatic potential of PC-3. We conclude that the stromal tissue architecture maintained in the implanted tumor played a critical role in tumor growth and progression.

L23 ANSWER 14 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:50664 BIOSIS
DN PREV199800050664
TI Mitomycin C and cisplatin increase survival in a human pancreatic cancer metastatic model.
AU Tomikawa, Moriaki; Kubota, Tetsuro; Matsuzaki, Shinjiro Wilson; Takahasi, Shin; Kitajima, Masaki; Moosa, A. R.; Hoffman, Robert M. (1)
CS (1) AntiCancer Inc., 7917 Ostrow St., San Diego, CA 92111 USA
SO Anticancer Research, (***Sept.-Oct., 1997***) Vol. 17, No. 5A, pp. 3623-3626.
ISSN: 0250-7005.
DT Article
LA English
AB Pancreatic cancer is one of the most intractable of all human cancers. We have previously developed a patient-like model of human pancreatic cancer by ***surgical*** ***orthotopic*** ***implantation*** (SOI). After SOI of the human tumor xenograft PAN-12-JCK into the tail of the nude mouse pancreas, mitomycin C (MMC) and cisplatin (DDP) were administered intraperitoneally at a dose of 4 and 6 mg/kg, respectively,

on day 7. The mice were observed for 95 days. There was a statistically significant increase in disease-free and overall survival rates in the MMC- and MMC+ DDP-treated groups. Local tumor growth was eliminated only in the group treated with MMC + DDP. Hepatic metastasis and peritoneal disseminations were completely inhibited by MMC but not DDP. This study demonstrates the usefulness of the SOI model of pancreatic cancer to study the differential efficacy of agents affecting primary tumor growth metastasis and survival, thus presenting an opportunity for the discovery of new agents for this highly resistant cancer.

L23 ANSWER 15 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:50623 BIOSIS
DN PREV199800050623
TI Antimetastatic activity of the new platinum analog Pt(cis-dach) (DPPE). 2NO3 in a metastatic model of human bladder cancer.
AU Chang, Sung-Goo (1); Kim, Jin Il; Jung, Jee-Chang; Rho, Young-Soo; Lee, Kyung-Tae; An, Zili; Wang, Xiaoen; Hoffman, Robert M.
CS (1) Dep. Urol., Kyung Hee Univ., Med. Cent., 1, Hoegidong Dongdaemun ku, Seoul 130-702 South Korea
SO Anticancer Research, (***Sept.-Oct., 1997***) Vol. 17, No. 5A, pp. 3239-3242.
ISSN: 0250-7005.
DT Article
LA English
AB ***Surgical*** ***orthotopic*** ***implantation*** (SOI) of histologically intact human RT-4 bladder tumor tissue in nude mice resulted in local growth, invasion, regional extension and metastases as well as distant metastases to other organ sites and lymph nodes, thus mimicking the bladder cancer patient. This metastatic bladder tumor animal model was treated with two doses of new platinum analog (Pt(cis-dach) (DPPE)cntdot2NO3) for the evaluation of antimetastatic efficacy compared to two doses of cisplatinum. Unlike the untreated control group or the group treated with the low dose of cisplatinum, there were no metastases in either the high or low-dose platinum-analog-treated groups and the high-dose cisplatinum-treated group. The results obtained with this patient-like nude-mouse model of bladder cancer indicate that the new platinum analog appears to be a valuable lead compound with antimetastatic efficacy and clinical potential.

L23 ANSWER 16 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:417629 BIOSIS
DN PREV199799716832
TI Fertile seed and rich soil: The development of clinical relevant models of human cancer by ***surgical*** ***orthotopic*** ***implantation*** of intact tissue.
AU Hoffman, Robert M.
CS AntiCancer Inc., San Diego, CA USA
SO Teicher, B. A. [Editor]. Cancer Drug Discovery and Development, (1997) No. 2, pp. 127-144. Cancer Drug Discovery and Development; Anticancer drug development guide: Preclinical screening, clinical trials, and approval. Publisher: Humana Press Inc. Suite 808, 999 Riverview Drive, Totowa, New Jersey 07512, USA.
ISBN: 0-89603-461-5.
DT Book
LA English

L23 ANSWER 17 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:403386 BIOSIS
DN PREV199799709589
TI Metastatic patterns of lung cancer visualized live and in process by green fluorescence protein expression.
AU Chishima, Takashi; Miyagi, Yohei; Wang, Xiaoen; Baranov, Eugene; Tan, Yuying; Shimada, Hiroshi; Moossa, A. R.; Hoffman, Robert M. (1)
CS (1) AntiCancer Inc., 7917 Ostrow St., San Diego, CA 92111 USA
SO Clinical & Experimental Metastasis, (1997) Vol. 15, No. 5, pp. 547-552.
ISSN: 0262-0898.
DT Article
LA English
AB We demonstrate here the visualization of human lung cancer metastasis live and in process in nude mice by green fluorescent protein (GFP) expression. The human lung adenocarcinoma cell line Anip 973 stably transfected with the humanized GFP-S65T cDNA was selected for very bright green fluorescence. GFP-transfected lung cancer cells were initially inoculated subcutaneously in nude mice. Five weeks after transplantation, the resulting tumor had reached over 1 cm in diameter and had very bright GFP fluorescence. Fragments of subcutaneous tumor were implanted onto the visceral pleura of the left lung of nude mice by ***surgical*** ***orthotopic*** ***implantation*** (SOI) of histologically-intact tissue via transverse thoracotomy. The ipsilateral resulting tumor was highly fluorescent due to GFP expression. GFP expression allowed the visualization of the advancing margin of the ipsilateral tumor into the fresh normal lung tissue. Lymphogenous and direct-seeding metastases in the pulmonary hilum, cervical lymph nodes, the mediastinum and contralateral pleural cavity and contralateral lung in the SOI-treated mice were brightly visualized by GFP expression in fresh tissue. GFP-transfected and untransfected tumor had similar metastatic characteristics suggesting that GFP expression had no effect on metastasis itself. The results with the GFP-transfected tumor cells, combined with the use of SOI, demonstrate a fundamental advance in the visualization and study of lung cancer metastasis in process.

L23 ANSWER 18 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:402869 BIOSIS
DN PREV199799709072
TI Visualization of the metastatic process by green fluorescent protein expression.
AU Chishima, Takashi; Miyagi, Yohei; Wang, Xiaoen; Tan, Yuying; Shimada, Hiroshi; Moossa, Ar; Hoffman, Robert M. (1)
CS (1) AntiCancer,Inc., 7917 Ostrow St., San Diego, CA 92111 USA
SO Anticancer Research, (1997) Vol. 17, No. 4A, pp. 2377-2384.
ISSN: 0250-7005.
DT Article
LA English
AB We demonstrate here the visualization of the cancer metastatic process in live tissue in vivo by green fluorescent protein (GFP) expression. The human lung adenocarcinoma cell-line Anip 973 was transfected with the humanized GFP-S65T cDNA and stable high-level GFP-expressing transfectants were established GFP transfectants were initially inoculated subcutaneously in nude mice. Five weeks after transplantation, when the tumor had reached 1.2 cm in diameter, fragments of subcutaneously tumor were implanted onto the visceral pleura of nude mice by ***surgical*** ***orthotopic*** ***implantation*** (SOI) as a spontaneous metastatic modeL GFP expressing cells were injected intravenously in nude mice as an experimental hematogenous metastasis modeL Mice were sacrificed four and eight weeks after treatment. At eight weeks, SOI-treated mice had lymphogenous (3/4 mice) and direct seeding (3/4) metastasis in the pulmonary hilum, cervical lymph nodes, the mediastinum and contralateral pleural cavity as detected by GFP expression in live tissue. All intravenously injected mice had metastases in the lung (4/4) and some of them had metastases in the brain (2/4) and other organs (1/4) as detected by GFP expression in fresh tissue. Some of the lung metastases produced by intravenous injection remained as dormant small colonies even eight weeks after treatment. These different metastatic patterns after SOI and intravenous injection visualized by GFP expression indicates that initial steps of the metastatic cascade influence the subsequent progression of metastasis.

L23 ANSWER 19 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:261466 BIOSIS
DN PREV199799568069
TI Cancer invasion and micrometastasis visualized in live tissue by green fluorescent protein expression.
AU Chishima, Takashi; Miyagi, Yohei; Wang, Xiaoen; Yamaoka, Hiroyuki; Shimada, Hiroshi; Moossa, A. R.; Hoffman, Robert M. (1)
CS (1) AntiCancer Inc., 7917 Ostrow St., San Diego, CA 92111 USA
SO Cancer Research, (1997) Vol. 57, No. 10, pp. 2042-2047.
ISSN: 0008-5472.
DT Article
LA English
AB We report the establishment of stable, high-level green fluorescent protein (GFP)-expressing cell lines in vitro that permit the detection and visualization of distant micrometastases when they are implanted orthotopically in nude mice. Chinese hamster ovary cells were transfected with the dicistronic expression vector containing the humanized GFP cDNA. A stable GFP-expressing clone was selected in 1.5 mu-M methotrexate in vitro and injected s.c. in nude mice. Stable high-level expression of GFP was maintained in the s.c. growing tumors. To use GFP expression for metastasis studies, fragments of s.c. growing tumor, which are comprised of GFP-expressing cells, were implanted by ***surgical*** ***orthotopic*** ***implantation*** in the ovary of nude mice. Subsequent micrometastases were detected in systemic organs and could be visualized by GFP fluorescence in the lung, liver, and other organs down to the single-cell level. With this fluorescent tool, we detected and visualized for the first time tumor cells at the microscopic level in fresh viable tissue in their normal host organ. Confocal microscopy further enabled us to study physiologically relevant patterns of invasion and micrometastasis.

L23 ANSWER 20 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:206774 BIOSIS
DN PREV199799505977
TI Conversion of highly malignant colon cancer from an aggressive to a controlled disease by oral administration of a metalloproteinase inhibitor.
AU An, Zili; Wang, Xiaoen; Willmott, Neville; Chander, Surinder K.; Tickle, Simon; Docherty, Andrew J. P.; Mountain, Andrew; Millican, Andrew T.; Morphy, Richard; Porter, John R.; Epemolu, R. Ola; Kubota, Tetsuro; Moossa, A. R.; Hoffman, Robert M. (1)
CS (1) 7917 Ostrow St., San Diego, CA 92111 USA
SO Clinical & Experimental Metastasis, (1997) Vol. 15, No. 2, pp. 184-195.
ISSN: 0262-0898.
DT Article
LA English
AB In this study, we describe the activity of CT1746, an orally-active synthetic MMP inhibitor that has a greater specificity for gelatinase A, gelatinase B and stromelysin than for interstitial collagenase and matrilysin, in a nude mouse model that better mimics the clinical development of human colon cancer. The model is constructed by ***surgical*** ***orthotopic*** ***implantation*** (SOI) of

histologically-intact tissue of the metastatic human colon tumor cell line Co-3. Animals were gavaged with CT1746 twice a day at 100 mg/kg for 5 days after the SOI of Co-3 for 43 days. In this model CT1746 significantly prolonged the median survival time of the tumor-bearing animals from 51 to 78 days. Significant efficacy of CT1746 was observed on primary tumor growth (32% reduction in mean tumor area at day 36), total spread and metastasis (6/20 treated animals had no detectable spread and metastasis at autopsy compared to 100% incidence of secondaries in control groups). Efficacy of CT1746 could also be seen on reducing tumor spread and metastasis to individual organ sites such as the abdominal wall, cecum and lymph nodes compared to vehicle and untreated controls. We conclude that chronic administration of a peptidomimetic MMP inhibitor via the oral route is feasible and results in inhibition of solid tumor growth, spread and metastasis with increase in survival in this model of human cancer, thus converting aggressive cancer to a more controlled indolent disease.

L23 ANSWER 21 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:46695 BIOSIS
DN PREV199799345898
TI Clinical course of human epithelial-type malignant pleural mesothelioma replicated in an orthotopic transplant nude mouse model.
AU Colt, H. G. (1); Astoul, P.; Wang, X.; Yi, E. S.; Boutin, C.; Hoffman, R. M.
CS (1) Div. Pulmonary Care, UCSD, La Jolla, CA USA
SO Clinical & Experimental Metastasis, (1996) Vol. 14, No. SUPPL. 1, pp. 42. Meeting Info.: Sixth International Congress of the Metastasis Research Society Gent, Belgium September 8-11, 1996
ISSN: 0262-0898.
DT Conference; Abstract; Conference
LA English

L23 ANSWER 22 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:46694 BIOSIS
DN PREV199799345897
TI High lung and lymph node metastatic targeting of the human prostate carcinoma cell line PC-3 surgically orthotopically implanted in nude mice.
AU An, Z.; Wang, X.; Hoffman, R. M.
CS AntiCancer Inc., 7917 Ostrow St., San Diego, CA 92111 USA
SO Clinical & Experimental Metastasis, (1996) Vol. 14, No. SUPPL. 1, pp. 42. Meeting Info.: Sixth International Congress of the Metastasis Research Society Gent, Belgium September 8-11, 1996
ISSN: 0262-0898.
DT Conference; Abstract; Conference
LA English

L23 ANSWER 23 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:46693 BIOSIS
DN PREV199799345896
TI The identification of highly metastatic human stomach tumor cancer cell lines by ***surgical*** ***orthotopic*** ***implantation*** in nude mice.
AU An, Z. (1); Wang, X. (1); Hosokawa, S.; Hirakawa, Y.; Nagaike, K.; Hoffman, R. M. (1)
CS (1) AntiCancer Inc., 7917 Ostrow St., San Diego, CA 92111 USA
SO Clinical & Experimental Metastasis, (1996) Vol. 14, No. SUPPL. 1, pp. 41. Meeting Info.: Sixth International Congress of the Metastasis Research Society Gent, Belgium September 8-11, 1996
ISSN: 0262-0898.
DT Conference; Abstract; Conference
LA English

L23 ANSWER 24 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:46618 BIOSIS
DN PREV199799345821
TI ***Surgical*** ***orthotopic*** ***implantation*** (SOI): A new approach to develop clinically-relevant models of human metastatic cancer in immunodeficient rodents.
AU Hoffman, Robert M.
CS AntiCancer Inc., 7917 Ostrow Street, San Diego, CA 92111 USA
SO Clinical & Experimental Metastasis, (1996) Vol. 14, No. SUPPL. 1, pp. 12-13.
Meeting Info.: Sixth International Congress of the Metastasis Research Society Gent, Belgium September 8-11, 1996
ISSN: 0262-0898.
DT Conference; Abstract
LA English

L23 ANSWER 25 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:563824 BIOSIS
DN PREV199799293180
TI Interferon gamma is highly effective against orthotopically-implanted human pleural adenocarcinoma in nude mice.
AU An, Zili; Wang, Xiaoen; Astoul, Philippe; Danays, T.; Moossa, A. R.; Hoffman, Robert M. (1)
CS (1) Anticancer Inc., 7917 Ostrow St, San Diego, CA 92111 USA
SO Anticancer Research, (1996) Vol. 16, No. 5A, pp. 2545-2551.
ISSN: 0250-7005.
DT Article
LA English
AB The efficacy of recombinant human gamma interferon (rh IFN-gamma) was evaluated for the treatment of human pleural adenocarcinoma in a patient-like nude mice model which is constructed by ***surgical*** ***orthotopic*** ***implantation*** (SOI) of histologically-intact human tumor tissue. The human non-small-cell lung cancer cell line H-460 was used for the study. Gamma interferon was tested in three different dosages (25, 000 U, 50, 000 U and 100,000 U) versus an untreated control through i.p. injection twice a day for five days, which was started 48 hours after SOI; The results showed that IFN-gamma can prolong the survival time of the tumor-beating animals. The symptoms and signs of hypoxia such as restricted physical activity and cyanosis due to primary tumor growth in the thoracic cavity as well as cachexia developed much earlier in the control than in the IFN-gamma-treated mice. The mice in the control group had succumbed by day-23 after tumor implantation, however at that time 67% of the mice in the 100,000 U-treated group, 15% of the mice in the 50,000 U-treated group, and 16% of the mice in the 25,000 U-treated group were still alive. The orthotopically-transplanted tumor grew rapidly and metastasized to the lung and liver in the untreated control. In the IFN-gamma-treated groups both primary tumor growth and metastasis were reduced, probably accounting for the increased survival rate. The results demonstrated dose-dependent efficacy of IFN-gamma in suppressing symptomology, primary tumor growth, invasiveness and metastasis of the human lung cancer cell line H 460, and increased survival of the tumor-bearing animals. These results suggest clinical trials of IFN-gamma should begin for treatment of pleural adenocarcinoma for which there is no current effective therapy.

L23 ANSWER 26 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:335744 BIOSIS
DN PREV199699058100
TI A clinical nude mouse metastatic model for highly malignant human pancreatic cancer.
AU An, Zili; Wang, Xiaoen; Kubota, Tetsuro; Moossa, A. R.; Hoffman, Robert M.
CS 7917 Ostrow St., San Diego, CA 92111 USA
SO Anticancer Research, (1996) Vol. 16, No. 2, pp. 627-631.
ISSN: 0250-7005.
DT Article
LA English
AB Pancreatic cancer is a highly aggressive and treatment-refractory cancer. A clinically-relevant animal model is necessary to develop therapy for metastatic pancreatic cancer. In this study we evaluated the efficacy of mitomycin C (MMC) and 5-FU against the human pancreatic adenocarcinoma cell line PAN-12 in an orthotopic human metastatic pancreatic cancer nude mice model. The model is constructed by ***surgical*** ***orthotopic*** ***implantation*** (SOI) of histologically intact tumor tissue in the tail portion of the pancreas near the spleen. PAN-12 grew very aggressively in the control group of nude mice with extensive local invasion and distant metastasis to various organs with a propensity for the lung but to other organs as well, including the liver, kidney and regional and distant lymph nodes. In a striking effect none of the mice in the MMC-treated group developed tumor. Although mice in the 5-FU treated group survived statistically significantly longer than those in the untreated control, the overall incidence of metastasis in these mice was equivalent to those in the control. However no liver or kidney metastases were found in the 5-FU treated animals perhaps accounting in part for their longer survival. This "clinical" nude mouse model of highly metastatic pancreatic cancer can now be used to discover new effective agents for this disease.

L23 ANSWER 27 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:335457 BIOSIS
DN PREV199699057813
TI Clinical course of human epithelial-type malignant pleural mesothelioma replicated in an orthotopic-transplant nude mouse model.
AU Colt, Henri G. (1); Astoul, Philippe; Wang, Xiaoen; Yi, Eunhee S.; Boutin, Christian; Hoffman, Robert M.
CS (1) Pulmonary Special Procedures Unit, CSD Medical Cent., 200 West Arbor Dr., San Diego, CA 92103 USA
SO Anticancer Research, (1996) Vol. 16, No. 2, pp. 633-639.
ISSN: 0250-7005.
DT Article
LA English
AB Malignant pleural mesothelioma is an aggressive tumor that is essentially unresponsive to standard medical and surgical therapies. Little is actually known about its biologic response to therapeutic interventions, in part because of a lack of a "patient-like" animal tumor model. Most experimental models thus far have been derived from inhalation or inoculation of asbestos fibers into animal subjects or by subcutaneous transplantation of human mesothelial cell lines into nude mice. These models are not representative of clinical malignant pleural mesothelioma. In this report, an animal model of human pleural malignant mesothelioma obtained by orthotopic transplantation of intact pleural tumor tissue into athymic nude mice is described. Pleural tumor obtained by thoracoscopy from a patient with epithelial-type malignant pleural mesothelioma was implanted as intact tissue by ***surgical*** ***orthotopic*** ***implantation*** (SOI) into the tight pleural cavity of nude mice. Animals were sacrificed when moribund or 6 months after implantation. Tumor growth and regional spread in the mice evaluated at postmortem examination mimicked the clinical pattern of progression of human disease. Histologic findings and the immunohistochemical profile were similar to

those demonstrated on examination of thoracoscopic parietal pleural biopsy specimens and post-mortem examination of the original patient's tumor. This "patient-like" nude mouse model of epithelial-type malignant pleural mesothelioma, phenotypically similar to the original human tumor, should facilitate future investigation of tumorigenesis and metastatic potential of this neoplasm. The model should serve as a basis for assessing the impact of experimental and existing therapy on malignant mesothelioma.

L23 ANSWER 28 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:254610 BIOSIS
DN PREV199698810739
TI Liver colonization capability govern metastatic potential.
AU Kuo, T.-H. (1); Kubota, T. (1); Watanabe, M. (1); Furukawa, T. (1); Teramoto, T. (1); Ishibiki, K. (1); Kitajima, M. (1); Moossa, A.; Penman, S.; Hoffman, R. M.
CS (1) Dep. Surg., Keio Univ., Tokyo Japan
SO Proceedings of the American Association for Cancer Research Annual Meeting, (1996) Vol. 37, No. 0, pp. 72.
Meeting Info.: 87th Annual Meeting of the American Association for Cancer Research Washington, D.C., USA April 20-24, 1996
ISSN: 0197-016X.
DT Conference
LA English

L23 ANSWER 29 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:79269 BIOSIS
DN PREV199698651404
TI Liver colonization competence governs colon cancer metastasis.
AU Kuo, Tsong-Hong; Kubota, Tetsuro (1); Watanabe, Masahiko; Furukawa, Toshiharu; Teramoto, Tatuso; Ishibiki, Kyuya; Kitajima, Masaki; Moossa, A. Rahim; Penman, Sheldon; Hoffman, Robert M.
CS (1) Dep. Surg., Sch. Medicine, Keio Univ., 35 Shinanomachi, Shinjuki-ju, Tokyo 160 Japan
SO Proceedings of the National Academy of Sciences of the United States of America, (1995) Vol. 92, No. 26, pp. 12085-12089.
ISSN: 0027-8424.
DT Article
LA English
AB Tumors that metastasize do so to preferred target organs. To explain this apparent specificity, Paget, gt 100 years ago, formulated his seed and soil hypothesis; i.e., the cells from a given tumor would "seed" only favorable "soil" offered by certain organs. The hypothesis implies that cancer cells must find a suitable "soil" in a target organ sbd i.e., one that supports colonization sbd for metastasis to occur. We demonstrate in this report that ability of human colon cancer cells to colonize liver tissue governs whether a particular colon cancer is metastatic. In the model used in this study, human colon tumors are transplanted into the nude mouse colon as intact tissue blocks by ***surgical*** ***orthotopic*** ***implantation*** . These implanted tumors closely simulate the metastatic behavior of the original human patient tumor and are clearly metastatic or nonmetastatic to the liver. Both classes of tumors were equally invasive locally into tissues and blood vessels. However, the cells from each class of tumor behave very differently when directly injected into nude mouse livers. Only cells from metastasizing tumors are competent to colonize after direct intrahepatic injection. Also, tissue blocks from metastatic tumors affixed directly to the liver resulted in colonization, whereas no colonization resulted from nonmetastatic tumor tissue blocks even though some growth occurred within the tissue block itself. Thus, local invasion (injection) and even adhesion to the metastatic target organ (blocks) are not sufficient for metastasis. The results suggest that the ability to colonize the liver is the governing step in the metastasis of human colon cancer.

L23 ANSWER 30 OF 32 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 1999159193 EMBASE
TI Orthotopic transplant mouse models with green fluorescent protein-expressing cancer cells to visualize metastasis and angiogenesis.
AU Hoffman R.M.
CS R.M. Hoffman, AntiCancer, Inc., 7917 Ostrow Street, San Diego, CA 92111, United States. all@anticancer.com
SO Cancer and Metastasis Reviews, (1998) 17/3 (271-277).
Refs: 36
ISSN: 0167-7659 CODEN: CMRED4
CY Netherlands
DT Journal; General Review
FS 016 Cancer
026 Immunology, Serology and Transplantation
LA English
SL English
AB There have been major efforts in metastasis research in recent years, especially on the role of angiogenesis in the metastatic process. Much of the information in this area has been obtained from model systems that are not representative of clinical cancer. The technique of ***surgical*** ***orthotopic*** ***implantation*** (SOI) has allowed the development of clinically relevant metastatic models of human cancer in immunodeficient rodents such as the nude and SCID mouse. In order to allow direct visualization of the metastatic process, we took advantage of the green fluorescent protein (GFP) of the jellyfish, Aequorea victoria. A series of cancer cell lines have been stably transfected with vectors containing humanized GFP cDNA. To utilize GFP expression for metastasis studies, fragments of subcutaneously growing tumor, which were comprised of GFP-expressing cells, were implanted by SOI in nude mice. Subsequent metastases were visualized in systemic organs by GFP fluorescence in the lung, liver, bones, brain and other organs down to the single-cell level. With this fluorescent tool, we detected and visualized for the first time tumor cells at the microscopic level in fresh viable tissue in their normal host organs even in the live animal. Angiogenesis is readily visualized in the transplanted GFP-expressing tumors in real time in situ in the live animal using simple laparotomy and fluorescent techniques. The results with the GFP-transfected tumor cells, combined with the use of SOI, demonstrate a fundamental advance to visualize and study cancer metastasis and the role of angiogenesis and other factors in the metastatic process.

L23 ANSWER 31 OF 32 CAPLUS COPYRIGHT 2002 ACS
AN 1999:324927 CAPLUS
DN 131:155471
TI Green fluorescent protein to visualize cancer progression and metastasis
AU Hoffman, Robert M.
CS AntiCancer, Inc., San Diego, CA, 92111, USA
SO Methods in Enzymology (***1999***), 302(Green Fluorescent Protein), 20-31
CODEN: MENZAU; ISSN: 0076-6879
PB Academic Press
DT Journal
LA English
AB Chinese hamster ovary cells and the human lung adenocarcinoma cell lines ANIP 973 and H-460 were transfected with the dicistronic expression vector contg. the humanized green fluorescent protein (GFP) cDNA. Stable GFP-expressing clones were selected in 1.5 .mu.M methotrexate in vitro and injected s.c. in nude mice. Stable, high-level expression of GFP was maintained in the s.c. growing tumors. To utilize GFP expression for metastasis studies, fragments of s.c. growing tumor, which were composed of GFP-expressing cells, were implanted by ***surgical*** ***orthotopic*** ***implantation*** (SOI) in the ovary and lung, resp., of nude mice. Subsequent micrometastases were visualized in systemic organs by GFP fluorescence in the lung, liver, brain, skeleton, and other organs down to the single-cell level. With this fluorescence tool, we detected and visualized for the first time tumor cells at the microscopic level in fresh viable tissue in their normal host organ. The results with the GFP-transfected tumor cells, combined with the use of SOI, demonstrate a fundamental advance in the visualization and study of lung cancer metastasis in process. Lung tissue seeded with GFP-expressing ANIP 973 human lung carcinoma cells was incubated in three-dimensional sponge-gel matrix-supported histoculture. Tumor progression was continuously visualized by GFP fluorescence in the same individual cultures over a 52-day period, during which time the tumors spread throughout the histocultured lung. Histoculture tumor colonization was selective for the growth of lung cancer cells on lung tissue, as no growth occurred on histocultured mouse liver tissue, as also obsd. in vivo. The ability to support selective organ colonization in histoculture and visualize tumor progression by GFP fluorescence allows the in vitro study of tumor progression in situ. (c) 1999 Academic Press.
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 32 OF 32 CAPLUS COPYRIGHT 2002 ACS
AN 1999:138451 CAPLUS
DN 130:336070
TI Fertile seed and rich soil: the development of clinically relevant models of human cancer by ***surgical*** ***orthotopic*** ***implantation*** of intact tissue
AU Hoffman, Robert M.
CS Anticancer Inc., San Diego, CA, USA
SO Anticancer Drug Development Guide (***1997***), 127-144. Editor(s): Teicher, Beverly A. Publisher: Humana, Totowa, N. J.
CODEN: 67LMAC
DT Conference; General Review
LA English
AB A review with 131 refs. An historical and anal. outline of the development of animal models of human cancer and their potential to understand and treat cancer metastasis is presented.
RE.CNT 138 THERE ARE 138 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>
=> s hGFP-S65T
L24 10 HGFP-S65T

=> dup rem l24
PROCESSING COMPLETED FOR L24
L25 4 DUP REM L24 (6 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L25 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 2001:366742 CAPLUS
DN 134:363676
TI Metastasis models using green fluorescent protein (gfp) as a marker
IN Tan, Yuying; Chishima, Takashi

PA Anticancer, Inc., USA
SO U.S., 10 pp., Cont.-in-part of U.S. Ser. No. 49,544.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6235968	B1	20010522	US 1998-67734	19980428
US 6232523	B1	20010515	US 1997-848539	19970428
US 6235967	B1	20010522	US 1998-49544	19980327
US 6251384	B1	20010626	US 1999-226856	19990107
US 2002026649	A1	20020228	US 2001-870268	20010529

PRAI US 1997-848539 A2 19970428
US 1998-49544 A2 19980327
US 1998-67734 A2 19980428
US 1999-226856 A1 19990107
AB A method to follow the progression of metastasis of a primary tumor, which method comprises removing fresh organ tissues from a vertebrate subject which has been modified to contain tumor cells that express GFP and observing the excised tissues for the presence of fluorescence is disclosed. The fluorescence can also be monitored by observing the tissues in situ. Vertebrate subjects which contain GFP producing tumors are useful models to study the mechanism of metastasis. In addn., subjects already harboring tumors can be treated so as to modify the endogenous tumors to contain GFP. This permits clin. applications. Finally, by injecting a contrast dye into a subject harboring a GFP-labeled tumor, angiogenesis in the tumor can be obsd. directly.
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 1997:295486 BIOSIS
DN PREV199799594689
TI Green fluorescent protein variants as markers of retroviral-mediated gene transfer in primary hematopoietic cells and cell lines.
AU Bierhuizen, Marti F. A.; Westerman, Yvonne; Visser, Truoi P.; Wognum, Albertus W.; Wagemaker, Gerard
CS Inst. Hematol., Erasmus Univ. Rotterdam, PO Box 1738, 3000 DR Rotterdam Netherlands
SO Biochemical and Biophysical Research Communications, (1997) Vol. 234, No. 2, pp. 371-375.
ISSN: 0006-291X.
DT Article
LA English
AB Retroviral vectors are widely used for the introduction of exogenous genetic material into hematopoietic cells. Here we report the generation of retroviral vectors containing the Aequorea victoria green fluorescent protein (GFP) gene and improved versions thereof. Murine fibroblasts transduced with the mutant GFP genes demonstrated a distinct green fluorescent signal in fluorescence-activated cell sorter (FACS) analysis. The relative intensities of peak green fluorescence observed with different GFP mutants were in the order EGFP gt ***hGFP*** (***S65T***) gt GFP-PTS1 or TSFGP gt wildtype GFP (wtGFP). Furthermore, GFP-PTS1 expressions was observed in murine (3T3, Rat2, and freshly-cultured bone marrow) and human (K562) cells transduced with the corresponding retroviral vector. The GFP-PTS1 positive phenotype could be selected for by FACS and appeared to be stable for at least 1 month in murine fibroblasts and human K562 cells. Therefore, these GFP variants are convenient selectable markers to monitor retroviral-mediated gene transfer and expression in mammalian hematopoietic cells.

L25 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 1997:87594 BIOSIS
DN PREV199799379307
TI Tracking and quantitation of retroviral-mediated transfer using a completely humanized, red-shifted green fluorescent protein gene.
AU Muldoon, R. R.; Levy, J. P.; Kain, S. R.; Kitts, P. A.; Link, C. J., Jr. (1)
CS (1) Gene Therapy Prog., HGTR1, 1415 Woodland Ave., Des Moines, IA 50309 USA
SO Biotechniques, (1997) Vol. 22, No. 1, pp. 162-164, 166-167.
ISSN: 0736-6205.
DT Article
LA English
AB We have developed murine retroviral vectors (RVs) containing an optimized green fluorescent protein (GFP) gene to study retroviral gene transfer and expression in living cells. We used the codon "humanized", "red-shifted" GFP gene, hGFPS65T, a gain of function variant of the wild-type GFP from the jellyfish Aequorea victoria. We cloned the ***hGFP*** - ***S65T*** gene into the RV plasmid pLNCX (pLNChG65T). A stable amphotropic RV-producer cell line (VPC), designated LVChG65T VPC, was generated that exhibited bright fluorescence in greater than 95% of the cells. Human A375 melanoma cells and IGROV ovarian carcinoma cells transduced from LNCh-G65T
VPC demonstrated high levels of fluorescence. The expression of a single integrated ***hGFP*** - ***S65T*** gene in eukaryotic cells provides a powerful tool to study gene transfer expression and functional studies in vitro and in vivo.

L25 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
AN 1997:396015 BIOSIS
DN PREV199799695218
TI Live astrocytes visualized by green fluorescent protein in transgenic mice.
AU Zhuo, Lang (1); Sun, Biao; Zhang, Chuan-Li; Fine, Alan; Chiu, Shing-Yan; Messing, Albee (1)
CS (1) Dep. Pathobiological Sciences, Sch. Veterinary Med., Univ. Wisconsin-Madison, Madison, WI 53706 USA
SO Developmental Biology, (1997) Vol. 187, No. 1, pp. 36-42.
ISSN: 0012-1606.
DT Article
LA English
AB Green fluorescent protein (***hGFP*** - ***S65T***) was expressed in transgenic mice under the control of the astrocyte-specific glial fibrillary acidic protein (GFAP) promoter. Tissues from two independent transgenic lines were characterized by Northern blot analysis and by confocal microscopy. The expression pattern in these two lines was identical in all tissues examined, and similar to that found previously with a lacZ transgene driven by the same promoter. Bright fluorescence was observed in the cell bodies and processes of unfixed or fixed astrocytes, using both whole mount and brain slice preparations, from multiple areas of the central nervous system. However, in contrast to GFAP-lacZ transgenics, retinal Muller cells expressed the GFP transgene in response to degeneration of neighboring photoreceptors. These data indicate that the 2.2-kb hGFAP promoter contains sufficient regulatory elements to direct expression in Muller cells, and that GFP is a suitable reporter gene for use in living preparations of the mammalian nervous system. Such mice should prove useful for studies of dynamic changes in astrocyte morphology during development, and in response to physiological and pathological conditions.

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          frequency
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 NEWS 8 Mar 22 TRCTHERMO no longer available
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          and USPATFULL
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IFIUDB
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ZCAPLUS
 NEWS 17 Apr 22 BIOSIS Gene Names now available in TOXCENTER
 NEWS 18 Apr 22 Federal Research in Progress (FEDRIP) now available

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          CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
          AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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=> s humaniz? (3a) CRE
L1          3 HUMANIZ? (3A) CRE

=> dup rem l1
PROCESSING COMPLETED FOR L1
L2          1 DUP REM L1 (2 DUPLICATES REMOVED)

=> d bib abs

L2  ANSWER 1 OF 1  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS
INC.DUPLICATE 1
AN  1996:332418  BIOSIS
DN  PREV199699054774
TI  Humanized prion protein knock-in by Cre-induced site-specific
    recombination in the mouse.
AU  Kitamoto, Tetsuyuki (1); Nakamura, Kenji; Nakao, Kazuki; Shibuya, Satoshi;
    Shin, Ryong-Woon; Gondo, Yoichi; Katsuki, Motoya; Tateishi, Jun
CS  (1) Dep. Neurol. Sci., Tohoku Univ. Sch. Med., Sendai Japan
SO  Biochemical and Biophysical Research Communications, (1996) Vol. 222, No.
    3, pp. 742-747.
    ISSN: 0006-291X.
DT  Article
LA  English
AB  To establish humanized mice with a knock-in (gene replacement) technique,
    we constructed a targeting vector which consists of the human prion
    protein and the loxP sequences. The introduced human prion protein with
    the loxP system in the embryonic stem cells was transmitted through the
    mouse germ line. Transient expression of Cre recombinase in the fertilized
    eggs resulted in the prion protein  ***humanized***  mice. The
     ***Cre***  -loxP-mediated gene replacement is a simple and efficient
    method which is generally applicable to make humanized animal models.


=> s modif? (3a) cre
L3          51 MODIF? (3A) CRE

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4          22 DUP REM L3 (29 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 22 ANSWERS - CONTINUE? Y/(N):y

L4  ANSWER 1 OF 22  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS
INC.DUPLICATE
    1
AN  2001:504285  BIOSIS
DN  PREV200100504285
TI  Delivery of the Cre recombinase by a self-deleting lentiviral vector:
    Efficient gene targeting in vitro.
AU  Pfeifer, Alexander; Brandon, Eugene P.; Kootstra, Neeltje; Gage, Fred H.;
    Verma, Inder M. (1)
CS  (1) Salk Institute, La Jolla, CA, 92037: verma@salk.edu USA
SO  Proceedings of the National Academy of Sciences of the United States of
    America, (September 25, 2001) Vol. 98, No. 20, pp. 11450-11455. print.
    ISSN: 0027-8424.
DT  Article
LA  English
SL  English
AB  The Cre recombinase (Cre) from bacteriophage P1 is an important tool for
    genetic engineering in mammalian cells. We constructed lentiviral vectors
    that efficiently deliver Cre in vitro and in vivo. Surprisingly, we found
    a significant reduction in proliferation and an accumulation in the G2/M
    phase of Cre-expressing cells. To minimize the toxic effect of Cre, we
    designed a lentiviral vector that integrates into the host genome,
    expresses Cre in the target cell, and is subsequently deleted from the
    genome in a Cre-dependent manner. Thus, the activity of Cre terminates its
    own expression (self-deleting). We showed efficient modification of target
    genes in vitro and in the brain after transduction with the self-deleting
    vectors. In contrast to sustained Cre expression, transient expression of
    Cre from the self-deleting vector induced significantly less cytotoxicity.
    Such a self-deleting Cre vector is a promising tool for the induction of
    conditional gene  ***modifications***  with minimal  ***Cre***
    toxicity in vivo.

L4  ANSWER 2 OF 22  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS
INC.
AN  2002:38491  BIOSIS
DN  PREV200200038491
TI  Development of lentiviral vectors encoding Cre recombinase for conditional
    genetic modification in the mouse.
AU  Brandon, E. P. (1); Pfeifer, A. (1); Ikawa, M. (1); Schaffer, D. (1);
    Verma, I. M. (1); Gage, F. H. (1)
CS  (1) Lab of Genetics, Salk Inst Biolog Studies, La Jolla, CA USA
SO  Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2, pp. 2345.
    print.
    Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San
    Diego, California, USA November 10-15, 2001
    ISSN: 0190-5295.
DT  Conference
LA  English
AB  The Cre-loxP system is a versatile tool for conditional genetic
    modification with the power to activate or inactivate a gene in vivo with
    spatial and temporal precision. A gene that has been tagged with the 34 bp
    loxP DNA sequences can be recombined and consequently functionally
     ***modified***  when  ***Cre***  recombinase (  ***Cre***  ) is
    expressed. To develop an effective new Cre delivery system we are
    utilizing human immunodeficiency virus (HIV)-based lenitviral vectors.
    Lentivirus is attractive as a Cre delivery system because (1) high titer
    virus can be readily produced, (2) the virus can infect high percentages
    of post-mitotic neurons in vivo, (3)no deleterious neurobiological effects
    of the virus per se have been observed, and (4) unlike germ line
    transgenic Cre systems, it does not require any interbreeding of mice. A
    third generation self-inactivating lentiviral vector encoding Cre fused to
    a nuclear localization signal has been developed (lenti-Cre). The virus
    was initially tested and found to be effective in a Cre-loxP reporter cell
    line that carries a beta-galactosidase (b-gal) cassette. For in vivo
    testing, virus was injected into various brain regions of the ROSA26R
    reporter mice that express b-gal in any cell that has undergone Cre-loxP
    recombination. Within one week of injection of lenti-Cre into the
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hippocampus b-gal was already detectable. Three weeks after a single injection, a majority of cells within a transduced volume one mm around the injection site were b-gal positive. Thus lenti-Cre is highly efficacious for recombining loxP-modified genes in the brain.

L4 ANSWER 3 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
2
AN 2001:121812 BIOSIS
DN PREV200100121812
TI Downregulation of fasting-induced cAMP response element-mediated gene induction by leptin in neuropeptide Y neurons of the arcuate nucleus.
AU Shimizu-Albergine, Masami; Ippolito, Danielle L.; Beavo, Joseph A. (1)
CS (1) Department of Pharmacology, School of Medicine, University of Washington, Seattle, WA, 98195: beavo@u.washington.edu USA
SO Journal of Neuroscience, (February 15, 2001) Vol. 21, No. 4, pp. 1238-1246. print.
ISSN: 0270-6474.
DT Article
LA English
SL English
AB States of increased metabolic demand such as fasting modulate hypothalamic neuropeptide gene expression and decrease circulating leptin levels. This study tested the hypotheses that fasting stimulates gene induction mediated by cAMP response element (CRE)-dependent increases in gene transcription and that fasting-induced decreases in leptin can regulate this CRE-mediated gene induction. Using C57BL/6J mice transgenic for a CRE-lacZ construct, an immunocytochemical study showed that fasting activated reporter gene expression in the hypothalamic arcuate nucleus (Arc) in a small subset of neurons and increased phosphorylation of CRE binding protein. The increase of beta-galactosidase expression caused by fasting was inhibited by a protein kinase A inhibitor, Rp-8-Br-cAMPS, when the compound was microinjected into the medial basal hypothalamus, and enhanced by intraperitoneal injection of selective phosphodiesterase inhibitors. In situ hybridization studies showed that neuropeptide Y (NPY) mRNA levels increased in the Arc during fasting, whereas proopiomelanocortin (POMC) mRNA levels decreased. Double labeling of mRNA
and beta-galactosidase immunoreactivity in the fasted brain indicated that the subpopulation of the neurons expressing beta-galactosidase all produced NPY but not POMC. To study the possible involvement of decreased circulating leptin during starvation on CRE-mediated gene induction, leptin was administered intraperitoneally to fasted mice. Leptin significantly attenuated both beta-galactosidase expression and NPY gene expression stimulated by fasting, suggesting that leptin inhibits fasting-stimulated NPY gene expression at least in part through downregulation of CRE-mediated gene induction in the Arc. Leptin-induced ***modification*** of ***CRE*** -mediated gene induction in the Arc may play an essential role in the central regulation of feeding behavior and energy expenditure.

L4 ANSWER 4 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:557296 BIOSIS
DN PREV200100557296
TI Advances in the biosafety research of non-target DNA in transgenic plants.
AU Dong Zhi-Feng (1); Ma Rong-Cai; Peng Yu-Fa; Guan Hua-Shi
CS (1) Ocean University of Qingdao, Qingdao, 266003 China
SO Acta Botanica Sinica, (July, 2001) Vol. 43, No. 7, pp. 661-672. print.
ISSN: 0577-7496.
DT Article
LA Chinese
SL Chinese; English
AB The biosafety of genetically engineered plants has been of concernment in society and science in recent years. The issue of 35S promoter of CaMV has been contentious because of its wide use in plant genetic engineering. The debate on the safety and potential risks of the 35S promoter will be discussed here. Some of concerns are expressed about the dissemination of antibiotic-resistance genes and vector backbone sequences. Various methods and strategies are currently being developed for the marker gene excision and elimination of vector backbone sequences from transgenic plants. In this review, the CRE/lox system which could get rid of the marker genes and vector backbone sequences will be discussed in detail. Advances in the research of the safety assessment of genetically ***modified*** plants using the ***CRE*** /lox system will also be described.

L4 ANSWER 5 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
3
AN 2001:420984 BIOSIS
DN PREV200100420984
TI Efficient elimination of selectable marker genes from the plastid genome by the CRE-lox site-specific recombination system.
AU Corneille, Sylvie; Lutz, Kerry; Svab, Zora; Maliga, Pal (1)
CS (1) Waksman Institute, Rutgers, State University of New Jersey, 190 Frelinghuysen Road, Piscataway, NJ, 08854-8020: maliga@waksman.rutgers.edu
USA
SO Plant Journal, (July, 2001) Vol. 27, No. 2, pp. 171-178. print.
ISSN: 0960-7412.
DT Article
LA English
SL English
AB Incorporation of a selectable marker gene during transformation is essential to obtain transformed plastids. However, once transformation is accomplished, having the marker gene becomes undesirable. Here we report on adapting the P1 bacteriophage CRE-lox site-specific recombination system for the elimination of marker genes from the plastid genome. The system was tested by the elimination of a negative selectable marker, codA, which is flanked by two directly oriented lox sites (>codA>). Highly efficient elimination of >codA> was triggered by introduction of a nuclear-encoded plastid-targeted CRE by Agrobacterium transformation or via pollen. Excision of >codA> in tissue culture cells was frequently accompanied by a large deletion of a plastid genome segment which includes the tRNA-ValUAC gene. However, the large deletions were absent when cre was introduced by pollination. Thus pollination is our preferred protocol for the introduction of cre. Removal of the >codA> coding region occurred at a dramatic speed, in striking contrast to the slow and gradual build-up of transgenic copies during plastid transformation. The nuclear cre gene could subsequently be removed by segregation in the seed progeny. The ***modified*** ***CRE*** -lox system described here will be a highly efficient tool to obtain marker-free transplastomic plants.

L4 ANSWER 6 OF 22 MEDLINE
AN 2001381583 MEDLINE
DN 21132574 PubMed ID: 11236673
TI The LoxP/ ***CRE*** system and genome ***modification*** .
AU Wilson T J; Kola I
CS Centre for Functional Genomics and Human Disease, Monash University, Melbourne, Australia.
SO METHODS IN MOLECULAR BIOLOGY, (2001) 158 83-94. Ref: 14
Journal code: BU3; 9214969. ISSN: 1064-3745.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200107
ED Entered STN: 20010709
Last Updated on STN: 20010709
Entered Medline: 20010705

L4 ANSWER 7 OF 22 MEDLINE
AN 2001347820 MEDLINE
DN 21304075 PubMed ID: 11410679
TI A single vector containing ***modified*** ***cre*** recombinase and LOX recombination sequences for inducible tissue-specific amplification of gene expression.
AU Kaczmarczyk S J; Green J E
CS Transgenic Oncogenesis Group, Laboratory of Cell Regulation and Carcinogenesis, National Cancer Institute, Bethesda, MD 20892, USA.
SO NUCLEIC ACIDS RESEARCH, (2001 Jun 15) 29 (12) E56-6.
Journal code: O8L; 0411011. ISSN: 1362-4962.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200107
ED Entered STN: 20010730
Last Updated on STN: 20010730
Entered Medline: 20010726
AB The selective alteration of the genome using Cre recombinase to target the rearrangement of genes flanked by LOX recognition sequences has required the use of two separate genetic constructs in trans, one containing cre and the other containing the gene of interest flanked by LOX sites. We have developed a strategy in which both the cre recombinase gene and LOX recombination sites may be cloned within a single vector in cis. This method uses a ***modified*** form of ***Cre*** (CREM) that contains alterations to the 5' region including the introduction of a Kozak consensus sequence and insertion of a functional intron. This system allows for the inducible, tissue-specific activation or inactivation of gene expression in a single vector and can be utilized for the 300-fold amplification of gene expression from a weak promoter. This approach can be applied to targeting strategies for generating genetically altered mice and gene therapy.

L4 ANSWER 8 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
4
AN 2001:140751 BIOSIS
DN PREV200100140751
TI Characterization of the upstream enhancer of the rat sodium/iodide symporter gene.
AU Chun, J. T. (1); Di Lauro, R.
CS (1) Department of Biochemistry and Molecular Biology, Stazione Zoologica 'Anton Dohrn', Villa Comunale, 80121, Napoli: chun@alpha.szn.it Italy
SO Experimental and Clinical Endocrinology & Diabetes, (2001) Vol. 109, No. 1, pp. 23-26. print.
ISSN: 0947-7349.
DT Article
LA English
SL English
AB We previously demonstrated the presence of an enhancer that is located between nucleotides -2264 and -2495 in the 5' flanking region of the rat sodium/iodide symporter (NIS) gene (Ohno et al., 1999). When attached to

NIS or heterologous promoters, this 232 bp fragment, which we call NUE, is able to stimulate transcription in a thyroid-specific and cAMP-dependent manner. A paired-domain transcription factor Pax8 binds to this enhancer and can stimulate the transcription in non-thyroid cells that do not normally support the NUE activities. Cotransfection of PKA, a downstream effector of cAMP, further potentiates the Pax8-mediated transactivation. However, this transcriptional machinery containing pax8 seems to require contributions from the neighboring cis-acting element that is similar to CRE/AP-1 consensus sequences. ***Modification*** of this putative ***CRE*** /AP-1 site not only represses the NUE transcriptional activities by 90% in FRTL-5 cells, but also nullifies the synergistic effect of PKA on pax8-mediated transactivation in HeLa cells. In this report, we have further characterized the putative CRE/AP-1 site within the NIS upstream enhancer using gel mobility shift assay. An oligonucleotide probe with NIS CRE/AP-1 sequence produced complex binding patterns in both FRTL-5 and HeLa cell, reflecting the presence of diverse classes of binding factors. When compared with CRE or AP-1 elements in other genes, the mobility shift pattern of NIS CRE/AP-1 was similar to those of collagenase TRE, c-Jun TRE, and somatostatin CRE, but the relative intensities of the binding complexes were quite different. This observation raises a possibility that the NIS CRE/AP-site is regulated by a novel mechanism.

L4 ANSWER 9 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:174449 BIOSIS
DN PREV200100174449
TI Production of antibodies using Cre-mediated site-specific recombination.
AU Jakobovits, Ay; Zsebo, Krisztina M. (1)
CS (1) Woodside, CA USA
ASSIGNEE: Abgenix, Inc.; Japan Tobacco Inc., Tokyo, Japan
PI US 6091001 July 18, 2000
SO Official Gazette of the United States Patent and Trademark Office Patents, (July 18, 2000) Vol. 1236, No. 3, pp. No Pagination. e-file.
ISSN: 0098-1133.
DT Patent
LA English
AB A method to produce a cell expressing an antibody from a genomic sequence of the cell comprising a ***modified*** immunoglobulin locus using ***Cre*** -mediated site-specific recombination is disclosed. The method involves first transfecting an antibody-producing cell with a homology-targeting vector comprising a lox site and a targeting sequence homologous to a first DNA sequence adjacent to the region of the immunoglobulin loci of the genomic sequence which is to be converted to a modified region, so the first lox site is inserted into the genomic sequence via site-specific homologous recombination. Then the cell is transfected with a lox-targeting vector comprising a second lox site suitable for Cre-mediated recombination with the integrated lox site and a modifying sequence to convert the region of the immunoglobulin loci to the modified region. This conversion is performed by interacting the lox sites with Cre in vivo, so that the modifying sequence inserts into the genomic sequence via Cre-mediated site-specific recombination of the lox sites. Also disclosed are a form of the method used to produce a cell expressing a ***modified*** antibody molecule using ***Cre*** -mediated site-specific recombination, and antibody-producing cells obtainable by the disclosed methods. Class-switching modifications of human antibodies produced in murine hybridoma cells are exemplified.

L4 ANSWER 10 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
5
AN 2000:403320 BIOSIS
DN PREV200000403320
TI Molecular characterization at the RNA and gene levels of U3 snoRNA from a unicellular green alga, Chlamydomonas reinhardtii.
AU Antal, M.; Mougin, A.; Kis, M.; Boros, E.; Steger, G.; Jakab, G.; Solymosy, F.; Branlant, C. (1)
CS (1) MAEM, UMR CNRS-UHP 7567, Universite de Nancy I, F-54506, Vandoeuvre-les-Nancy Cedex France
SO Nucleic Acids Research, (August 1, 2000) Vol. 28, No. 15, pp. 2959-2968. print.
ISSN: 0305-1048.
DT Article
LA English
SL English
AB A U3 snoRNA gene isolated from a Chlamydomonas reinhardtii (Cre) genomic library contains putative pol III-specific transcription signals similar to those of RNA polymerase III-specific small nuclear (sn)RNA genes of higher plants. The 222 nt long Cre U3 snoRNA was immunoprecipitated by anti-gamma-mpppN antisera, but not by anti-m2,2,7G antibodies, supporting the notion that it is a RNA polymerase III transcript. Tagged Cre U3 snoRNA gene constructs were expressed in Cre cells. Results of chemical and enzymatic structure probing of Cre U3 snoRNA in solution and of DMS ***modification*** of ***Cre*** U3 snoRNA under in vivo conditions revealed that the two-hairpin structure of the 5'-domain that is found in solution is no longer detected under in vivo conditions. The observed differences can be explained by the formation of several base pair interactions with the 18S and 5'-ETS parts of the pre-rRNA. A model that involves five intermolecular helices is proposed.

L4 ANSWER 11 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
6
AN 2001:101849 BIOSIS
DN PREV200100101849
TI An engineered lox sequence containing part of a long terminal repeat of HIV-1 permits Cre recombinase-mediated DNA excision.
AU Lee, Young-sam; Kim, Sung-tae; Kim, Gyoung-won; Lee, Minhyung; Park, Jong-sang (1)
CS (1) Department of Chemistry, Seoul National University, Shilim-dong San 56-1, Kwanak-gu, Seoul, 151-742: pfjspark@plaza.snu.ac.kr South Korea
SO Biochemistry and Cell Biology, (2000) Vol. 78, No. 6, pp. 653-658. print.
ISSN: 0829-8211.
DT Article
LA English
SL English; French
AB In our previous report, one 34-bp sequence from a long terminal repeat (LTR) of human immunodeficiency virus type 1 (HIV-1) clone, loxLTR-1, was proposed as a target site for site-specific excision by ***modified*** ***Cre*** recombinase. To support this suggestion, an engineered lox sequence, designated loxIL1, was made. This variant lox has the corresponding sequence of loxLTR-1 at the spacer region and the last two bases of inverted repeat sequence. Through in vitro recombination assay, loxIL1 also allowed the wild-type Cre to specifically recombine the sequence. An in vitro DNA binding experiment with mutants CreK244R and CreK244L revealed that lysine 244 of Cre plays an important role in interaction with the engineered lox. This result suggests that loxLTR-1 would be a candidate for antiviral strategy using site-specific recombinase.

L4 ANSWER 12 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
7
AN 1999:263612 BIOSIS
DN PREV199900263612
TI Improved reporter strain for monitoring Cre recombinase-mediated DNA excisions in mice.
AU Mao, Xiaohong; Fujiwara, Yuko; Orkin, Stuart H. (1)
CS (1) Division of Hematology/Oncology, Department of Pediatrics, Children's Hospital and the Dana Farber Cancer Institute, Boston, MA, 02115 USA
SO Proceedings of the National Academy of Sciences of the United States of America, (April 27, 1999) Vol. 96, No. 9, pp. 5037-5042.
ISSN: 0027-8424.
DT Article
LA English
SL English
AB Effective use of conditional ***Cre*** recombinase-loxP gene ***modification*** requires ***Cre*** -expressing mouse strains with defined patterns of expression. To assess the in vivo functionality of Cre-expressing mice, we have engineered an improved reporter strain for monitoring Cre-mediated excisions. The beta-galactosidase-neomycin phosphotransferase fusion gene (betageo)-trapped ROSA26 locus was modified by gene targeting such that betageo is expressed only after Cre-mediated excision of loxP-flanked DNA sequences. betageo from the excised ROSA26 allele is expressed ubiquitously in embryos and adult mice. By mating the reporter strain with Cre-expressing transgenic mice, we have shown that the loxP-flanked ROSA26 allele is accessible to Cre during early embryogenesis, as well as in a specific hematopoietic lineage (T lymphocytes). This improved reporter strain should facilitate monitoring in vivo Cre-mediated excision events in a variety of experimental contexts.

L4 ANSWER 13 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
8
AN 1999:86783 BIOSIS
DN PREV199900086783
TI A novel mutant loxP containing part of long terminal repeat of HIV-1 in spacer region: Presentation of possible target site for antiviral strategy using site-specific recombinase.
AU Lee, Young-Sam; Park, Jong-Sang (1)
CS (1) Dep. Chem., Seoul Natl. Univ., Shilim-dong San 56-1, Kwanak-gu, Seoul 151-742 South Korea
SO Biochemical and Biophysical Research Communications, (Dec. 30, 1998) Vol. 253, No. 3, pp. 588-593.
ISSN: 0006-291X.
DT Article
LA English
AB A site-specific recombinase Cre is responsible for the recombination at a 34 hp loxP site. This system has been investigated for the antiviral strategy to excise proviral DNA from retrovirus-infected cells. It was reported that loxP sites could be inserted into long terminal repeat (LTR) of retrovirus to delete proviral DNA. To apply this system to human immunodeficiency virus type 1 (HIV-1) without inserting any DNA, one 34 hp sequence was selected from LTR of recombinant HIV-1 clone, loxLTR-1, based on sequence similarity between LTR and loxP, and sequence arrangement of 8 hp middle part in 34 bp LTR segment. When the 8 hp spacer region of loxP was changed into the corresponding middle part of loxLTR-1, this variant loxP would allow Cre to specifically recombine between themselves but not with wild-type loxP in vitro. This study suggests that site-specific excision of proviral DNA of HIV-1 could be catalyzed by the least ***modified*** ***Cre*** recognizing the loxLTR-1 sites.

L4 ANSWER 14 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
9

AN 1998:256562 BIOSIS
DN PREV199800256562
TI Modification of bacterial artificial chromosome clones using Cre recombinase: Introduction of selectable markers for expression in eukaryotic cells.
AU Kim, Su Young; Horrigan, Stephen K.; Altenhofen, Janine L.; Arbieva, Zarema H.; Hoffman, Ronald; Westbrook, Carol A. (1)
CS (1) Dep. Genet., Univ. Ill. at Chicago, Chicago, IL 60607 USA
SO Genome Research, (April, 1998) Vol. 8, No. 4, pp. 404-412.
ISSN: 1088-9051.
DT Article
LA English
AB Bacterial artificial chromosome clones (BACs) are widely used at present in human genome physical mapping projects. To extend the utility of these clones for functional genomic studies, we have devised a method to ***modify*** BACs using ***Cre*** recombinase to introduce a gene cassette into the loxP sequence, which is present in the vector portion of the BAC clone. Cre-mediated integration is site specific and thus maintains the integrity of the genomic insert sequences, while eliminating the steps that are involved in restriction digest-based DNA cloning strategies. The success of this method depends on the use of a DNA construct, RETRObac, which contains the reporter marker green fluorescent protein (GFP) and the selectable marker neomycin phosphotransferase (neo), but does not contain a bacterial origin of replication. BAC clones have been modified successfully using this method and the genomic insert shows no signs of deletions or rearrangements. Transfection efficiencies of the modified BACs into human or murine cell lines ranged from 1% to 6%. After culture in media containing G418 for 3 weeks, ~0.1% of cells previously sorted for GFP expression acquired stable antibiotic resistance. Introduction of a human BAC clone that contains genomic p53 sequences into murine NIH3T3 cells led to expression of human p53 mRNA as determined by RT-PCR, demonstrating that sequences contained on the BAC are expressed. We believe that GFP-neo modified BAC clones will be a valuable resource in efforts to study biological effects of known genes as well as in efforts to clone and analyze new genes and regulatory regions.

L4 ANSWER 15 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
10
AN 1998:302416 BIOSIS
DN PREV199800302416
TI Inducible gene targeting in mice using the Cre/lox system.
AU Sauer, Brian (1)
CS (1) Lab. Biochem. Metab., Natl. Inst. Diabetes Digestive Kidney Dis., Natl. Inst. Health, Build. 10, Room 9N119, Bethesda, MD 20892-1800 USA
SO Methods (Orlando), (April, 1998) Vol. 14, No. 4, pp. 381-392.
ISSN: 1046-2023.
DT Article
LA English
AB Molecular techniques now allow the design of precise genetic modifications in the mouse. Not only can defined nucleotide changes be engineered into the genome of the mouse, but genetic switches can be designed to target expression or ablation of any gene (for which basic molecular information is available) to any tissue at any defined time. These strategies promise to contribute substantially to an increased understanding of individual gene function in development and pathogenesis. A powerful tool, both for the design of such genetic switches and for speeding the creation of gene-***modified*** animals, is the ***Cre*** site-specific DNA recombinase of bacteriophage P1. Precise DNA rearrangements and genetic switches can be efficiently generated in a straightforward manner using Cre recombinase. In conjunction with inducible systems for controlling Cre expression and function, these recombination-based strategies are likely to have a profound impact on developmental biology and the generation of useful animal models of human disease.

L4 ANSWER 16 OF 22 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 97283419 EMBASE
DN 1997283419
TI Progress in defining the mechanism of action of antidepressants: Across receptors and into gene transcription.
AU Schwaninger M.; Weisbrod M.; Knepels W.
CS Dr. M. Schwaninger, Department of Neurology, University of Heidelberg, Im Neuenheimer Feld 400, 69120 Heidelberg, Germany
SO CNS Drugs, (1997) 8/3 (237-243).
Refs: 48
ISSN: 1172-7047 CODEN: CNDREF
CY New Zealand
DT Journal; General Review
FS 002 Physiology
030 Pharmacology
032 Psychiatry
037 Drug Literature Index
LA English
SL English
AB The mechanism of action of antidepressants is still unknown, The delayed onset of their therapeutic effect suggests that they act through an adaptive process. Recent research has demonstrated that neural plasticity and learning, which may underlie the induction of depression by repetitive psychosocial stress, involve gene transcription through the cyclic adenosine monophosphate (cAMP)- and calcium-responsive element (CRE) and
its cognate transcription factor CREB. By downregulating .beta.-adrenergic receptors linked to cAMP-formation and serotonin 5-HT2 receptors linked to intracellular calcium mobilisation and blocking voltage-dependent calcium channels, antidepressants can inhibit gene transcription through the ***CRE*** . Thus, ***modification*** of ***CRE*** -directed transcription may contribute to the therapeutic efficacy of antidepressants.

L4 ANSWER 17 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
11
AN 1995:408417 BIOSIS
DN PREV199598422717
TI Conditional site-specific recombination in mammalian cells using a ligand-dependent chimeric Cre recombinase.
AU Metzger, Daniel; Clifford, John; Chiba, Hideki; Chambon, Pierre
CS Inst. de Genet. et de Biologie Moleculaire et Cellulaire, Cent. Natl. de la Recherche Sci., Inst. Natl. de la Sante et de la Recherche Med., Universite Louis Pasteur, Coll. de France, 67404 Illkirch-Cedex, C.U. de Strasbourg France
SO Proceedings of the National Academy of Sciences of the United States of America, (1995) Vol. 92, No. 15, pp. 6991-6995.
ISSN: 0027-8424.
DT Article
LA English
AB We have developed a strategy to generate mutant genes in mammalian cells in a conditional manner by employing a fusion protein, Cre-ER, consisting of the loxP site-specific Cre recombinase linked to the ligand-binding domain of the human estrogen receptor. We have established homozygous retinoid X receptor alpha-negative (RXR-alpha-/-) F9 embryonal carcinoma cells constitutively expressing Cre-ER and have shown that estradiol or the estrogen agonist/antagonist 4-hydroxytamoxifen efficiently induced the recombinase activity, whereas no activity was detected in the absence of ligand or in the presence of the antiestrogen ICI 164,384. Furthermore, using a targeting vector containing a selection marker flanked by loxP sites, we have inactivated one retinoic acid receptor a allele in such a line, demonstrating that the presence of the recombinase does not inhibit homologous recombination. Combining this conditional site-specific recombination system with tissue-specific expression of ***Cre*** -ER may allow ***modification*** of the mammalian genome in vivo in a spatiotemporally regulated manner.

L4 ANSWER 18 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
12
AN 1996:21058 BIOSIS
DN PREV199698593193
TI Excision of specific DNA-sequences from integrated retroviral vectors via site-specific recombination.
AU Bergemann, Joerg; Kuehlcke, Klaus; Fehse, Boris; Ratz, Ilka; Ostertag, Wolfram; Lother, Heinz (1)
CS (1) Heinrich-Pette-Inst. fuer Experimentelle Virol. und Immunol., Univ. Hamburg, Martinistrasse 52, 20251 Hamburg Germany
SO Nucleic Acids Research, (1995) Vol. 23, No. 21, pp. 4451-4456.
ISSN: 0305-1048.
DT Article
LA English
AB Vectors for gene transfer and gene therapy were developed which combine the advantages of the integrase and recombinase systems. This was achieved by inserting two loxP sites for specific DNA excision into an MESV based retroviral vector. We show that this 'retroviral lox system' allows the infection of cells and the expression of transferred genes. In addition, we constructed an efficient retrovirus-based expression system for a ***modified*** ***Cre*** recombinase. Functional tests for DNA excision from integrated retroviral lox vectors were performed by the use of a negative selectable marker gene (thymidine kinase). Cre expression in cells infected with retroviral lox vectors and subsequent BrdU selection for cells in which site-specific recombination has occurred results in large numbers of independent cell clones. These results were confirmed by detailed molecular analysis. In addition we developed retroviral suicide vectors in which the enhancer/promoter elements of both LTRs were replaced by lox sequences. We show that lox-sequences located in the LTRs of retroviral vectors are stable during retroviral replication. Potential applications of this system would be the establishment of revertants of retrovirus-infected cells by controlled excision of nearly the complete proviral DNA.

L4 ANSWER 19 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
13
AN 1993:507543 BIOSIS
DN PREV199396131550
TI In vivo characterization of site-directed mutations in the promoter of the herpes simplex virus type 1 latency-associated transcripts.
AU Rader, Katherine A. (1); Ackland-Berglund, Cathleen E.; Miller, Judith Kelvin; Pepose, Jay S.; Leib, David A.
CS (1) Program Biomedical Sci., University California San Diego, La Jolla, CA 92037 USA
SO Journal of General Virology, (1993) Vol. 74, No. 9, pp. 1859-1869.
ISSN: 0022-1317.
DT Article
LA English
AB Transient expression assays in PC12 cells showed that the cAMP response element (CRE) and the TATA box of the herpes simplex virus type 1 latency-associated transcripts (LATs) promoter are essential for basal

expression. Recombinant viruses were generated containing site-specific mutations in these motifs. The abilities of these recombinants to replicate, express LATs and reactivate from latency were compared with wild-type and marker-rescued viruses in a murine ocular model. The acute replication of these TATA and CRE mutant viruses was at a level equivalent to their respective marker-rescued viruses. The reactivation of virus was unaffected by mutation in the TATA box as compared with wild-type or marker-rescued viruses. In situ hybridization of TATA box mutant virus-infected ganglia, however, showed threefold fewer LAT-positive neurons than wild-type virus-infected ganglia, with consistently weaker hybridization signals. Thus, this TATA box is required for normal expression of the LATs but not for efficient reactivation. The LATs CRE mutant reactivated with slightly but reproducibly reduced frequency and delayed kinetics relative to marker-rescued virus. By in situ hybridization, however, the percentage and intensity of LATs-positive neurons were found to be comparable for the CRE mutant- and wild-type virus-infected ganglia, suggesting that the CRE is dispensable for abundant LATs expression but that a reactivation function of the LATs may depend upon the presence of the ***CRE*** . Finally, using a ***modified*** assay for examining the timing of reactivation, we showed that the induction of viral reactivation by addition of exogenous cAMP can occur independently of the LATs.

L4 ANSWER 20 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
14
AN 1993:120115 BIOSIS
DN PREV199395064215
TI How tolerant are partial dose values? Some additional remarks on the concept of tolerance dose.
AU Jensen, J. M. (1); Melchert, U. H.; Ihnen, E.
CS (1) Klinik Strahlentherapie, Christian-Albrechts-Univ., Arnold-Heller-Strasse 9, D-2300 Kiel 1 Germany
SO Strahlentherapie und Onkologie, (1992) Vol. 168, No. 11, pp. 640-645. ISSN: 0179-7158.
DT Article
LA German
SL German; English
AB By means of the NSD-formula and its ***modifications*** (***CRE*** , TDF) evaluated from radiotherapy experience by Ellis, it is possible to estimate the acceptance of applied radiotherapy and fractionation scheme. Because the parameters of the Ellis-formula are calculated from patients data, they show a dispersion as usually in biological systems. These dispersions are considered as entrance error. In mathematical transformations errors are multiple according to the principle of superposition of errors. Especially when judging tolerance values of organs of risk the dispersion is quite important. The problem of dispersion of resulting partial tolerance values is demonstrated by some examples of clinical cases.

L4 ANSWER 21 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
15
AN 1982:159150 BIOSIS
DN BA73:19134
TI CUMULATIVE RADIATION EFFECT CALCULATIONS FOR DIFFERENT COMBINED RADIATION
TREATMENT SCHEMES OF UTERINE CERVICAL CARCINOMA.
AU VAYRYNEN T; KIVINIITTY K; KAUPPILA A
CS DEP. RADIOTHERAPY, UNIV. OULU, SF-OULU 22.
SO STRAHLENTHERAPIE, (1981) 157 (6), 396-399.
CODEN: STRAAA. ISSN: 0039-2073.
FS BA; OLD
LA English
AB The CRE [cumulative radiation effect] concept is not applicable to the assessment of the effect of combined radiotherapy when external and intracavitary radiations are given altenatively and with unequal doses. Because of the numerous recurrences, radiation treatment schemes for carcinoma cervix uteri had to be changed. On a theoretical basis, an attempt was made to acquire the same biological effect as Joslin with his method. In the comparison of different schemes we used a slightly ***modified*** approximate ***CRE*** and the nominal dose presented by Kellerer. The treatment schemes used and the methods for calculating the biological effect in combined treatment were presented. The applicability and compatibility of the above methods in comparing the effects of different combined radiation treatment schemes were examined.

L4 ANSWER 22 OF 22 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 80094289 EMBASE
DN 1980094289
TI The response of pig skin to single and fractionated high dose-rate and continuous low dose-rate 137Cs-irradiation. III. Re-evaluation of the CRE system and the TDF system according to the present findings.
AU Turesson I.; Notter G.
CS Dept. Radiat. Phys., Sahlgrenska Sjukh., Univ. Goteborg, S-413 45 Goteborg, Sweden
SO International Journal of Radiation Oncology Biology Physics, (1979) 5/10 (1773-1779).
CODEN: IOBPD3
CY United States
DT Journal
FS 014 Radiology
LA English
AB Application of the cumulative radiation effect (CRE) and time dose fractionation factors (TDF) systems on the dose-effect data from single and fractionated irradiation at high dose rate and continuous irradiation at low dose rate on pig skin revealed that significant corrections of these empirical models are necessary. There is evidence for ***modification*** of the ***CRE*** and TDF-formula for fractionated high dose-rate irradiation concerning late effects on normal tissue. The pig skin result indicated a value of the normalizing constant of 0.57 and 2.02 in the CRE and TDF-formulae for continuous irradiation instead of the proposed value of 0.80 and 1.57 respectively. The practical consequences for prediction of equivalent normal tissue reactions for fractionated high dose-rate and continuous low dose-rate irradiation by the CRE and TDF systems are elucidated.

=> s CRE (3a) recombinase?
L5 1684 CRE (3A) RECOMBINASE?

=> s sequence alter? or sequence modif?
L6 2134 SEQUENCE ALTER? OR SEQUENCE MODIF?

=> s l5 and l6
L7 0 L5 AND L6

=> s CRE
L8 8350 CRE

=> s l8 and l6
L9 0 L8 AND L6

=> d his

(FILE 'HOME' ENTERED AT 20:03:00 ON 08 MAY 2002)

FILE 'BIOSIS, MEDLINE, EMBASE' ENTERED AT 20:03:55 ON 08 MAY 2002
L1 3 S HUMANIZ? (3A) CRE
L2 1 DUP REM L1 (2 DUPLICATES REMOVED)
L3 51 S MODIF? (3A) CRE
L4 22 DUP REM L3 (29 DUPLICATES REMOVED)
L5 1684 S CRE (3A) RECOMBINASE?
L6 2134 S SEQUENCE ALTER? OR SEQUENCE MODIF?
L7 0 S L5 AND L6
L8 8350 S CRE
L9 0 S L8 AND L6

=> s mammal? codon
L10 16 MAMMAL? CODON

=> s mammal? (5a) codon
L11 214 MAMMAL? (5A) CODON

=> s l11 and l8
L12 8 L11 AND L8

=> dup rem l12
PROCESSING COMPLETED FOR L12
L13 3 DUP REM L12 (5 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L13 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 2002:184623 BIOSIS
DN PREV200200184623
TI Codon-improved ***Cre*** recombinase (iCre) expression in the mouse.
AU Shimshek, D. R.; Kim, J.; Huebner, M. R.; Spergel, D. J.; Buchholz, F.; Casanova, E.; Stewart, A. F.; Seeburg, P. H.; Sprengel, R. (1)
CS (1) Department of Molecular Neuroscience, Max-Planck Institute for Medical Research, Jahnstrasse 29, 69120, Heidelberg: sprengel@mpimf-heidelberg.mpg.de Germany
SO Genesis The Journal of Genetics and Development, (January, 2002) Vol. 32, No. 1, pp. 19-26. http://www.interscience.wiley.com/jpages/1526-954X/. print.
ISSN: 1526-954X.
DT Article
LA English
AB By applying the ***mammalian*** ***codon*** usage to ***Cre*** recombinase, we improved ***Cre*** expression, as determined by immunoblot and functional analysis, in three different mammalian cell lines. The improved ***Cre*** (iCre) gene was also designed to reduce the high CpG content of the prokaryotic coding sequence, thereby reducing the chances of epigenetic silencing in mammals. Transgenic iCre expressing mice were obtained with good frequency, and in these mice loxP-mediated DNA recombination was observed in all cells expressing iCre. Moreover, iCre fused to two estrogen receptor hormone binding domains for temporal control of ***Cre*** activity could also be expressed in transgenic mice. However, ***Cre*** induction after administration of tamoxifen yielded only low ***Cre*** activity. Thus, whereas efficient activation of ***Cre*** fusion proteins in the brain needs further improvements, our studies indicate that iCre should facilitate genetic experiments in the mouse.

L13 ANSWER 2 OF 3 MEDLINE DUPLICATE 2
AN 2001375437 MEDLINE
DN 21327164 PubMed ID: 11120274
TI A new ***Cre*** recombinase gene based on optimal ***codon*** usage in ***mammals*** : a powerful material for organ-specific gene targeting.
AU Koresawa Y; Miyagawa S; Ikawa M; Matsunami K; Yamada M; Okabe M; Shirakura R
CS Division of Organ Transplantation, Biomedical Research Center, Osaka University Graduate School of Medicine, and Genome Information Research Center, Osaka University, Suita, Osaka, Japan.
SO TRANSPLANTATION PROCEEDINGS, (2000 Nov) 32 (7) 2516-7. Journal code: WE9; 0243532. ISSN: 0041-1345.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200108
ED Entered STN: 20010806
Last Updated on STN: 20010806
Entered Medline: 20010802

L13 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
AN 2000:254172 BIOSIS
DN PREV200000254172
TI Synthesis of a new ***cre*** recombinase gene based on optimal ***codon*** usage for ***mammalian*** systems.
AU Koresawa, Yukie; Miyagawa, Shuji (1); Ikawa, Masahito; Matsunami, Katsuyoshi; Yamada, Mako; Shirakura, Ryota; Okabe, Masaru
CS (1) Division of Organ Transplantation, Biomedical Research Center, Osaka University Graduate School of Medicine, 2-2 Yamadaoka, Suita, Osaka, 565-0871 Japan
SO Journal of Biochemistry (Tokyo), (March, 2000) Vol. 127, No. 3, pp. 367-372. print.
ISSN: 0021-924X.
DT Article
LA English
SL English
AB The origin of the ***Cre*** recombinase gene is bacteriophage P1, and thus the ***codon*** usages are different from in ***mammals*** . In order to adapt this ***codon*** usage for ***mammals*** , we synthesized a "mammalian ***Cre*** recombinase gene" and examined its expression in Chinese hamster ovarian tumor (CHO) cells. Significant increases in protein production as well as mRNA levels were observed. When the recombination efficiency was compared using CHO cell transfectants having a cDNA containing loxP sites, the "mammalian ***Cre*** recombinase gene" recombined the loxP sites much more efficiently than the wild-type ***Cre*** recombinase gene.

=> d his

(FILE 'HOME' ENTERED AT 20:03:00 ON 08 MAY 2002)

FILE 'BIOSIS, MEDLINE, EMBASE' ENTERED AT 20:03:55 ON 08 MAY 2002
L1 3 S HUMANIZ? (3A) CRE
L2 1 DUP REM L1 (2 DUPLICATES REMOVED)
L3 51 S MODIF? (3A) CRE
L4 22 DUP REM L3 (29 DUPLICATES REMOVED)
L5 1684 S CRE (3A) RECOMBINASE?
L6 2134 S SEQUENCE ALTER? OR SEQUENCE MODIF?
L7 0 S L5 AND L6
L8 8350 S CRE
L9 0 S L8 AND L6
L10 16 S MAMMAL? CODON
L11 214 S MAMMAL? (5A) CODON
L12 8 S L11 AND L8
L13 3 DUP REM L12 (5 DUPLICATES REMOVED)

=> s l11 and py<1999
2 FILES SEARCHED...
L14 151 L11 AND PY<1999

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15 77 DUP REM L14 (74 DUPLICATES REMOVED)

=> d bib abs 1-10

L15 ANSWER 1 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 1999:39525 BIOSIS
DN PREV199900039525
TI Targeted delivery of DNA encoding cytotoxic proteins through high-affinity fibroblast growth factor receptors.
AU Hoganson, Diana K.; Chandler, Lois A.; Fleurbaaij, Graham A.; Ying, Wenbin; Black, Margaret E.; Doukas, John; Pierce, Glenn F.; Baird, Andrew; Sosnowski, Barbara A. (1)
CS (1) Selective Genetics Inc., 11035 Roselle St., San Diego, CA 92121 USA
SO Human Gene Therapy, (***Nov. 20, 1998***) Vol. 9, No. 17, pp. 2565-2575.
ISSN: 1043-0342.
DT Article
LA English
AB Nonviral DNA delivery strategies for gene therapy have generally been limited by a lack of specificity and efficacy. However, ligand-mediated endocytosis can specifically deliver DNA in vitro to cells bearing the appropriate cognate receptors. Similarly, in order to circumvent problems related to efficacy, DNA must encode proteins with high intrinsic activities. We show here that the ligand basic fibroblast growth factor (FGF2) can target FGF receptor-bearing cells with DNA encoding therapeutic proteins. Delivery of genes encoding saporin, a highly potent ribosomal inactivating protein, or the conditionally cytotoxic herpes simplex virus thymidine kinase, a protein that can kill cells by activating the prodrug ganciclovir, is demonstrated. The saporin gene was ***codon*** optimized for ***mammalian*** expression and demonstrated to express functional protein in a cell-free assay. FGF2-mediated delivery of saporin DNA or thymidine kinase DNA followed by ganciclovir treatment resulted in a 60 and 75% decrease in cell number, respectively. Specificity of gene delivery was demonstrated in competition assays with free FGF2 or with recombinant soluble FGF receptor. Alternatively, when histone H1, a ligand that binds to cell surface heparan sulfate proteoglycans ("low-affinity" FGF receptors), was used to deliver DNA encoding thymidine kinase, no ganciclovir sensitivity was observed. These findings establish the feasibility of using ligands such as FGF2 to specifically deliver genes encoding molecular chemotherapeutic agents to cells.

L15 ANSWER 2 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 1999:29522 BIOSIS
DN PREV199900029522
TI Isochore evolution in mammals: A human-like ancestral structure.
AU Galtier, Nicolas; Mouchiroud, Dominique (1)
CS (1) Centre National Recheche Scientifique UMR 5558, Biometrie Genet. Biol. Populations, Univ. Claude Bernad Lyon 1, 43 Boulevard 11 novembre 1918, 69622 Villeurbanne Cedex France
SO Genetics, (***Dec., 1998***) Vol. 150, No. 4, pp. 1577-1584.
ISSN: 0016-6731.
DT Article
LA English
AB ***Codon*** usage in ***mammals*** is mainly determined by the spatial arrangement of genomic G + G-content, i.e., the isochore structure. Ancestral G + C-content at third codon positions of 27 nuclear protein-coding genes of eutherian mammals was estimated by maximum-likelihood analysis on the basis of a nonhomogeneous DNA substitution model, accounting for variable base compositions among present day sequences. Data consistently supported a human-like ancestral pattern, i.e., highly variable G + C-content among genes. The mouse genomic structure-more narrow G + C-content distribution-would be a derived state. The circumstances of isochore evolution are discussed with respect to this result. A possible relationship between G + C-content homogenization in murid genomes and high mutation rate is proposed, consistent with the negative selection hypothesis for isochore maintenance in mammals.

L15 ANSWER 3 OF 77 MEDLINE DUPLICATE 3
AN 1998219452 MEDLINE
DN 98219452 PubMed ID: 9558741
TI Test system for quantification of stop ***codon*** suppression by selenocysteine insertion in ***mammalian*** cell lines.
AU Kollmus H; McCarthy J E; Flohe L
CS National Biotechnology Research Centre (GBF), Braunschweig, Germany.
SO ZEITSCHRIFT FUR ERNAHRUNGSWISSENSCHAFT, ***(1998)*** 37 Suppl 1 114-7.
Journal code: XTU; 0413632. ISSN: 0044-264X.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199805
ED Entered STN: 19980529
Last Updated on STN: 19980529
Entered Medline: 19980521
AB A convenient test system was designed to investigate the efficiencies of selenocysteine inserting sequences (SECIS) responsible for the cotranslational incorporation of selenocysteine into selenoproteins of mammals. It comprises an expression vector in which the lacZ and luc genes are separated by an in-frame TGA stop codon. The coding regions are followed by a multicloning region allowing exchange of putative SECIS elements. Stop codon suppression associated with selenocysteine incorporation is readily estimated on the basis of relative luciferase activity measurements, thus providing a measure of SECIS efficiency.

L15 ANSWER 4 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:94782 BIOSIS
DN PREV199900094782
TI Gene therapy for pancreatic carcinoma by tumour-antigen-transfected, autologous EBV-lymphoblasts: Mutated p21 and RAS as a model vaccine.
AU Kubuschok, B.; Cochlovius, C.; Hartmann, F.; Schmits, R.; Jung, W.; Pfreundschuh, M.
CS Dep. Internal Med. I, Univ. Saarland Med. Sch., D-66421 Homburg/Saar

Germany
SO Annals of Hematology, (1998) Vol. 77, No. SUPPL. 2, pp. S100.
Meeting Info.: Annual Congress of the German and Austrian Societies of Hematology and Oncology Frankfurt, Germany October 25-28, 1998 Austrian Society of Hematology and Oncology
. ISSN: 0939-5555.
DT Conference
LA English

L15 ANSWER 5 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
4
AN 1997:180061 BIOSIS
DN PREV199799471774
TI A cDNA encoding fish fibroblast growth factor-2, which lacks alternative translation initiation.
AU Hata, Jun-Ichiro; Takeo, Jiro; Segawa, Chisako; Yamashita, Shinya (1)
CS (1) Central Res. Lab., Nippon Suisan Kaisha Limited, 559-6 Kitanomachi, Hachioji, Tokyo 192 Japan
SO Journal of Biological Chemistry, (1997) Vol. 272, No. 11, pp. 7285-7289.
ISSN: 0021-9258.
DT Article
LA English
AB Here, we describe the isolation of a rainbow trout cDNA clone that contains the entire fibroblast growth factor-2 (FGF-2; basic FGF) coding region. Interestingly, the rainbow trout cDNA contains a translation stop codon just upstream of the primary initiating methionine codon and so cannot give rise to the longer forms of FGF-2 that are produced in mammals by alternative translation initiation at leucines farther upstream. Transfection of human FGF-2 cDNA into fish cells shows that fish cells can initiate protein synthesis at an upstream leucine CUG codon, surprisingly, however, synthesis is initiated only at the most 5' CUG and not at the two subsequent CUG codons or the methionine AUG ***codon*** also used in ***mammalian*** cells. Like other FGF-2 proteins, bacterially produced rainbow trout FGF-2 protein binds tightly to heparin-Sepharose and also promotes the proliferation of fibroblast cells. However, the protein differs from all others previously identified at amino acids 121-123, which are part of the proposed highly conserved receptor-binding domain. Comparisons of the efficacies of recombinant wild-type and mutant rainbow trout FGF-2 proteins demonstrate that these three amino acids are critical to the activity of FGF-2.

L15 ANSWER 6 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
5
AN 1998:45798 BIOSIS
DN PREV199800045798
TI Expression of chicken hepatic type I and type III iodothyronine deiodinases during embryonic development.
AU Van Der Geyten, Serge; Sanders, Jo. P.; Kaptein, Ellen; Darras, Veerle M.; Kuhn, Eduard R.; Leonard, Jack L.; Visser, Theo J. (1)
CS (1) Dep. Internal Med. III, Erasmus Univ. Med. Sch., Room Bd 234, P.O. Box 1738, 3000 DR Rotterdam Netherlands
SO Endocrinology, (***Dec., 1997***) Vol. 138, No. 12, pp. 5144-5152.
ISSN: 0013-7227.
DT Article
LA English
AB In embryonic chicken liver (ECL) two types of iodothyronine deiodinases are expressed: D1 and D3. D1 catalyzes the activation as well as the inactivation of thyroid hormone by outer and inner ring deiodination, respectively. D3 only catalyzes inner ring deiodination. D1 and D3 have been cloned from mammals and amphibians and shown to contain a selenocysteine (Sec) residue. We characterized chicken D1 and D3 complementary DNAs (cDNAs) and studied the expression of hepatic D1 and D3
messenger RNAs (mRNAs) during embryonic development. Oligonucleotides based on two amino acid sequences strongly conserved in the different deiodinases (NFGSCTSecP and YIEEAH) were used for reverse transcription-PCR of poly(A+) RNA isolated from embryonic day 17 (E17) chicken liver, resulting in the amplification of two 117-bp DNA fragments. Screening of an E17 chicken liver cDNA library with these probes led to the isolation of two cDNA clones, ECL1711 and ECL1715. The ECL1711 clone was 1360 bp long and lacked a translation start site. Sequence alignment showed that it shared highest sequence identity with D1s from other vertebrates and that the coding sequence probably lacked the first five nucleotides. An ATG start codon was engineered by site-directed mutagenesis, generating a mutant (ECL1711M) with four additional codons (coding for MGTR). The open reading frame of ECL1711M coded for a 249-amino acid protein showing 58-62% identity with ***mammalian*** D1s. An in-frame TGA ***codon*** was located at position 127, which is translated as Sec in the presence of a Sec insertion sequence (SECIS) identified in the 3'-untranslated region. Enzyme activity expressed in COS-1 cells by transfection with ECL1711M showed the same catalytic, substrate, and inhibitor specificities as native chicken D1. The ECL1715 clone was 1366 bp long and also lacked a translation start site. Sequence alignment showed that it was most homologous with D3 from other species and that the coding sequence lacked approximately the first 46 nucleotides. The deduced amino acid sequence showed 62-72% identity with the D3 sequences from other species, including a putative Sec residue at a corresponding position. The 3'-untranslated region of ECL1715 also contained a SECIS element. These results indicate that ECL1711 and ECL1715 are near-full-length cDNA clones for chicken D1 and D3 selenoproteins, respectively. The ontogeny of D1 and D3 expression in chicken liver was studied between E14 and 1 day after hatching (C1). D1 activity showed a gradual increase from E14 until C1, whereas D1 mRNA level remained relatively constant. D3 activity and mRNA level were highly significantly correlated, showing an increase from E14 to E17 and a strong decrease thereafter. These results suggest that the regulation of chicken hepatic D3 expression during embryonic development occurs predominantly at the pretranslational level.

L15 ANSWER 7 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:178960 BIOSIS
DN PREV199799470673
TI Human choline acetyltransferase mRNAs with different 5'-region produce a 69-kDa major translation product.
AU Misawa, Hidemi (1); Matsuura, Junkio; Oda, Yoshio; Takahashi, Ryosuke; Deguchi, Takeo
CS (1) Dep. Neurol., Tokyo Metropolitan Inst. Neurosci., 2-6, Musashidai, Fuchu City, Tokyo 183 Japan
SO Molecular Brain Research, (1997) Vol. 44, No. 2, pp. 323-333.
ISSN: 0169-328X.
DT Article
LA English
AB Choline acetyltransferase (ChAT, EC 2.3.1.6) is the biosynthetic enzyme for acetylcholine. We have previously shown that multiple ChAT mRNA species with different 5'-noncoding regions are expressed in the rat and mouse. However, the diversity of ChAT mRNA species in human has not completely been elucidated. In this work N1- and N2-type ChAT cDNAs were cloned from a human brain the rat, mouse and pig was replaced by ACG, which does not serve as an initiation codon for translation. In vitro translation and mRNAs (R-, N1-, N2- and M-types) are produced in human brain and spinal cord. In all human transcripts, the ATG initiation ***codon*** in ***mammalian*** expression analyses revealed that N1-, N2- and R-type mRNAs give rise to a single 69 kDa enzyme, while M-type mRNA produces both 82 and 69 kDa enzymes. The translation efficiency of M-type mRNA was lower than that of the other mRNA species. Moreover, the translation efficiency of human ChAT mRNAs was considerably lower than that of rat ChAT mRNA, suggesting that the ATG codons for human ChAT are unfavorable for translation initiation compared with the initiation codon for rat ChAT. These results provide rational explanations for the previous reports that human ChAT protein purified from the brain and placenta had 66-70 kDa molecular mass, and that ChAT activity in a single motor neuron of human was far lower than that of other vertebrates. Sequencing of monkey ChAT gene showed that the initiation ATG in rodent ChAT was also replaced by ACA in the monkey.

L15 ANSWER 8 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:47352 BIOSIS
DN PREV199800047352
TI Codon usage in Entamoeba histolytica, E. dispar and E. invadens.
AU Nozaki, Tomoyoshi (1); Asai, Takashi; Takeuchi, Tsutomu
CS (1) Dep. Tropical Med. Parasitology, Keio Univ., Sch. Med., 35 Shinanomachi, Shinjuku-ku, Tokyo 160 Japan
SO Parasitology International, (***July, 1997***) Vol. 46, No. 2, pp. 105-109.
ISSN: 1383-5769.
DT Article
LA English
AB We analyzed the frequencies of genetic codon usage of 68 non-redundant protein coding genes from the human-pathogenic E. histolytic (28 117 codons), 6 from the non-pathogenic E. dispar (1744 codons), and 4 from the reptilian E. invadens (933 codons). The A + U contents of the protein coding sequences from E. histolytica, E. dispar, and E. invadens were 67%, 66% and 58%, respectively. The nucleotide frequency in the third position was strongly biased toward A + U in E. histolytica and E. dispar (85% and 82%, respectively); the degree of the A + U bias was higher in the third position than that in the first or second position. In contrast, the nucleotide frequency in the third position was less biased in E. invadens (50% A + U) than in e. histolytica and E. dispar. Codon usage was biased in accordance with the A + U preference in the third position in E. histolytica and E. dispar. However, no apparent difference in the codon usage was found between E. histolytica and E. dispar. The codon usage in E. invadens was found less biased; the nucleotide biases observed in the third position of the synonymous codons for several amino acids including leucine, tyrosine, cysteine, and histidine of the E. histolytica and E. dispar genes were reversed or absent. The codon usage in Entamoeba species significantly differed from that in other amitochondrial protist, Giardia lamblia and Trichomonas vaginalis. Two sequences encoding ribosomal protein S10 and S27 showed significantly smaller codon biases than the rest of e. histolytica sequences, suggest that these ribosomal proteins might be under specific functional constraint of codon usage. The differences in the A + U content of the coding sequences and in the ***codon*** usage between the ***mammalian*** E. histolytica and e. dispar and the reptilian E. invadens suggested that the reptilian Entamoeba species were distantly related to the mammalian species. These results may aid in elucidating pressures that facilitate changes in the patterns of the genetic codon usage.

L15 ANSWER 9 OF 77 MEDLINE DUPLICATE 6
AN 97295237 MEDLINE
DN 97295237 PubMed ID: 9150879
TI Nonsense suppression in mammalian cells.
AU Kuchino Y; Muramatsu T

CS Biophysics Division of National Cancer Center Research Institute, Tokyo, Japan.
SO BIOCHIMIE, ***(1996)*** 78 (11-12) 1007-15. Ref: 32
Journal code: A14; 1264604. ISSN: 0300-9084.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199707
ED Entered STN: 19970805
Last Updated on STN: 19970805
Entered Medline: 19970721
AB Mammalian cells contain suppressor tRNAs that can translate nonsense codons such as UAG and UGA localized at a specific site of natural mRNAs. For translation of these nonsense codons, a specific secondary or tertiary structure of mRNAs located in the region surrounding the translatable nonsense ***codon*** is required. In ***mammalian*** cells, transcriptional expression of the tRNA gene encoding UAG suppressor glutamine tRNA is repressed by the binding of a nuclear protein to a specific site in the 5'-flanking region of the gene. Based on these findings, we discuss the translational regulation of nonsense codons in mammalian mRNAs.

L15 ANSWER 10 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
7
AN 1996:537585 BIOSIS
DN PREV199699259941
TI An enhanced green fluorescent protein allows sensitive detection of gene transfer in mammalian cells.
AU Zhang, Guohong (1); Gurtu, Vanessa; Kain, Steven R.
CS (1) Clontech Lab. Inc., 1020 East Meadow Circle, Palo Alto, CA 94303 USA
SO Biochemical and Biophysical Research Communications, (1996) Vol. 227, No. 3, pp. 707-711.
ISSN: 0006-291X.
DT Article
LA English
AB The green fluorescent protein (GFP) from the jellyfish Aequorea victoria has become an important marker of gene expression. However, the sensitivity of wild-type GFP has been below that of standard reporter proteins, such as beta-galactosidase, which utilize enzymatic amplification. To improve the detection of GFP in transfected mammalian cells, we have constructed a unique GFP variant which contains chromophore mutations that make the protein 35 times brighter than wild-type GFP, and is ***codon*** -optimized for higher expression in ***mammalian*** cells. These changes in the GFP coding sequence provide an enhanced GFP (EGFP) that greatly increases the sensitivity of the reporter protein. We show that the EGFP expression vector delivered into mammalian cells gives rise to bright fluorescence that is readily detectable following a 16-24 hr transfection interval. Visual detection of transfected cells with EGFP appears to be more sensitive than equivalent measurements with beta-galactosidase catalyzed conversion of the X-gal substrate. We conclude that EGFP allows sensitive and convenient detection of gene transfer in mammalian cells.

=> d bib abs 11-20

L15 ANSWER 11 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
8
AN 1996:236854 BIOSIS
DN PREV199698800983
TI Codon usage limitation in the expression of HIV-1 envelope glycoprotein.
AU Haas, Juergen; Park, Eun-Chung; Seed, Brian (1)
CS (1) Dep. Molecular Biol., Massachusetts General Hospital, Boston, MA 02114 USA
SO Current Biology, (1996) Vol. 6, No. 3, pp. 315-324.
ISSN: 0960-9822.
DT Article
LA English
AB Background: The expression of both the env and gag gene products of human immunodeficiency virus type 1 (HIV-1) is known to be limited by cis elements in the viral RNA that impede egress from the nucleus and reduce the efficiency of translation. Identifying these elements has proven difficult, as they appear to be disseminated throughout the viral genome. Results: Here, we report that selective codon usage appears to account for a substantial fraction of the inefficiency of viral protein synthesis, independent of any effect on improved nuclear export. The codon usage effect is not specific to transcripts of HIV-1 origin. Re-engineering the coding sequence of a model protein (Thy-1) with the most prevalent HIV-1 codons significantly impairs Thy-1 expression, whereas altering the coding sequence of the jellyfish green fluorescent protein gene to conform to the favored codons of highly expressed human proteins results in a substantial increase in expression efficiency. Conclusions: Codon-usage effects are a major impediment to the efficient expression of HIV-1 genes. Although mammalian genes do not show as profound a bias as do Escherichia coli genes, other proteins that are poorly expressed in ***mammalian*** cells can benefit from ***codon*** re-engineering.

L15 ANSWER 12 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
9
AN 1996:534947 BIOSIS
DN PREV199699257303
TI Molecular evolution and phylogenetic utility of the polyubiquitin locus in mammals and higher vertebrates.
AU Vrana, Paul B. (1); Wheeler, Ward C.
CS (1) Dep. Mol. Biol., Lewis Thomas Labs, Princeton Univ., Princeton, NJ 08544 USA
SO Molecular Phylogenetics and Evolution, (1996) Vol. 6, No. 2, pp. 259-269.
ISSN: 1055-7903.
DT Article
LA English
AB The product of ubiquitin genes is a small protein involved in intracellular sorting of other proteins. The locus consists of tandemly arrayed, uninterrupted copies of the gene. As several studies have noted, the Polyubiquitin locus is a model system for studying concerted evolution. While the protein is among the most conserved known, individual copies within an organism show variation in nucleotide sequence despite clear evidence of concerted evolution. When treated as individuals, repeats from a given locus form a monophyletic group. Furthermore adjacent copies often cluster, suggestive of the mechanism of concerted evolution. Due to this concerted evolution of repeats (and loci in organisms with multiple polyubiquitins), sequencing of heterogeneous PCR products consisting of all the repeats in a given organism may yield phylogenetic signal, as with other multicopy genes. We test this possibility through 22 original sequences using primers designed so that only tandem copies are amplified. Using these and previously published data, we further explore these phenomena in higher vertebrates and mammals in particular. We suggest that multiple locus duplications have occurred within ***mammals*** . Positional ***codon*** bias is strongly evident. We also find substitutional bias with regard to codon type. GC content of the locus appears to be generally high across vertebrates. Intraorganismal variation is tallied as an indication of frequency of change in codon position and transition/transversion ratios to further elucidate the tempo and mode of molecular evolution. Using these data, a weighting scheme for ubiquitin is also presented. Despite the gene's high GC content, transitional changes still appear more frequent. While the phylogenetic utility of ubiquitin does not appear great, its mechanistic insights seem far from exhausted.

L15 ANSWER 13 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
10
AN 1996:187631 BIOSIS
DN PREV199698743760
TI Synthesis of a modified gene encoding human ornithine transcarbamylase for expression in mammalian mitochondrial and universal translation systems: A novel approach towards correction of a genetic defect.
AU Wheeler, Vanessa C.; Prodromou, Chrisostomos; Pearl, Laurence H.; Williamson, Robert; Coutelle, Charles (1)
CS (1) Dep. Biochem. Mol. Genet., St. Mary's Hosp. Med. Sch., Norfolk Place, London W2 1PG UK
SO Gene (Amsterdam), (1996) Vol. 169, No. 2, pp. 251-255.
ISSN: 0378-1119.
DT Article
LA English
AB The mitochondrial (mt) genome is a potential means of gene delivery to human cells for therapeutic expression. As a first step towards this, we have synthesized a gene coding for mature human ornithine transcarbamylase (OTC) by recursive PCR using 18 oligodeoxyribonucleotides, each 70-80 nucleotides in length, with codons which should allow translation in accordance with both ***mammalian*** mt and universal ***codon*** usage. Flanking mt DNA sequences were incorporated which are designed to facilitate site-specific cloning into the mt genome. Expression of this human gene in Escherichia coli leads to an immunoreactive OTC product of the correct size and N-terminal amino-acid sequence, but which forms inclusion bodies and lacks enzymatic activity.

L15 ANSWER 14 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
11
AN 1996:282846 BIOSIS
DN PREV199699005202
TI Complete nucleotide sequences of the domestic cat (Felis catus) mitochondrial genome and a transposed mtDNA tandem repeat (Numt) in the nuclear genome.
AU Lopez, Jose V. (1); Cevario, Stanley; O'Brien, Stephen J.
CS (1) Smithsonian Tropical Res. Inst., Unit 0948, APO AA 34002-0948 USA
SO Genomics, (1996) Vol. 33, No. 2, pp. 229-246.
ISSN: 0888-7543.
DT Article
LA English
AB The complete 17,009-bp mitochondrial genome of the domestic cat, Felis catus, has been sequenced and conforms largely to the typical organization of previously characterized ***mammalian*** mtDNAs. ***Codon*** usage and base composition also followed canonical vertebrate patterns, except for an unusual ATC (non-AUG) codon initiating the NADH dehydrogenase subunit 2 (ND2) gene. Two distinct repetitive motifs at opposite ends of the control region contribute to the relatively large size (1559 hp) of this carnivore mtDNA. Alignment of the feline mtDNA

genome to a homologous 7946-bp nuclear mtDNA tandem repeat DNA sequence in
the cat, Numt, indicates simple repeat motifs associated with insertion/deletion mutations. Overall DNA sequence divergence between Numt and cytoplasmic mtDNA sequence was only 5.1%. Substitutions predominate at the third codon position of homologous feline protein genes. Phylogenetic analysis of mitochondrial gene sequences confirms the recent transfer of the cytoplasmic mtDNA sequences to the domestic cat nucleus and recapitulates evolutionary relationships between mammal species.

L15 ANSWER 15 OF 77 MEDLINE
AN 96293861 MEDLINE
DN 96293861 PubMed ID: 8722571
TI Sequence of the highly conserved gene encoding the human 54kDa subunit of signal recognition particle.
AU Patel S; Austen B
CS Department of Surgery, St. George's Hospital Medical School, London, UK.
SO DNA SEQUENCE, ***(1996)*** 6 (3) 167-70.
Journal code: A9H; 9107800. ISSN: 1042-5179.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X86373
EM 199610
ED Entered STN: 19961022
Last Updated on STN: 19961022
Entered Medline: 19961009
AB The complete sequence of the human gene encoding the 54kDa subunit of the signal recognition particle has been isolated from a cDNA library. Degenerate oligonucleotides based on the 5' and 3' coding region of the canine gene and a ***mammalian*** ***codon*** usage table, were used to amplify the sequence using PCR. The nucleotide sequence of the human gene shows that the human sequence shares a 95.8% nucleotide sequence homology and 100% amino acid sequence homology to it's canine counterpart. The sequence has been given the accession number X86373 in the EMBL database.

L15 ANSWER 16 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
12
AN 1996:438049 BIOSIS
DN PREV199699151655
TI Human lipoprotein lipase last exon is not translated, in contrast to lower vertebrates.
AU Arnault, F.; Etienne, J. (1); Noe, L.; Raisonnier, A.; Brault, D.; Harney, J. W.; Berry, M. J.; Tse, C.; Fromental-Ramain, C.; Hamelin, J.; Galibert, F.
CS (1) Lab. Biochim. et Biol. Moleculaire, Fac. Med. St.-Antoine-Tenon, 4 rue de la Chine, 75970 Paris Cedex 20 France
SO Journal of Molecular Evolution, (1996) Vol. 43, No. 2, pp. 109-115.
ISSN: 0022-2844.
DT Article
LA English
AB We have sequenced the first fish (zebrafish, Brachydanio rerio) lipoprotein lipase (LPL) cDNA clone. Similarities were found in ***mammalian*** LPL cDNA, but the ***codon*** spanning the last two exons (which is thus split by the last intron) is AGA (Arg) as opposed to TGA in mammals. Exon 10 is thus partially translated. These results were confirmed with rainbow trout (Oncorhynchus mykiss). We also investigated whether mammal TGA coded for selenocystein (SeCys), the 21st amino acid, but found that this was not the case: TGA does not encode SeCys but is a stop codon. It thus appears that the sense codon AGA (fish) has been transformed into a stop codon TGA (human) during the course of evolution. It remains to be determined if the "loss" of the C-terminal end of mammalian LPL protein has conferred an advantage in terms of LPL activity or, on the contrary, a disadvantage (e.g., susceptibility to diabetes or atherosclerosis).

L15 ANSWER 17 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
13
AN 1996:35467 BIOSIS
DN PREV199698607602
TI Context effects on misreading and suppression at UAG codons in human cells.
AU Phillips-Jones, Mary K.; Hill, Lindsey S. J.; Atkinson, Jeffifer; Martin, Robin (1)
CS (1) Blond McIndoe Cent., Queen Victoria Hosp., East Grinstead, Sussex RH19 3DZ UK
SO Molecular and Cellular Biology, (1995) Vol. 15, No. 12, pp. 6593-6600.
ISSN: 0270-7306.
DT Article
LA English
AB The effect of the 3' codon context on the efficiency of nonsense suppression in mammalian tissue culture cells has been tested. Measurements were made following the transfection of cells with a pRSVgal reporter vector that contained the classical Escherichia coli lacZ UAG allele YA559. The position of this mutation was mapped by virtue of its fortuitous creation of a CTAG MaeI restriction enzyme site. Determination of the local DNA sequence revealed a C fwdarw T mutation at codon 600 of the lacZ gene: CAG fwdarw TAG. Site-directed mutagenesis was Suppression of the amber-containing reporter was achieved by cotransfection with genes for human tRNA-Ser or tRNA-Glu UAG nonsense suppressors and by growth in the translational error-promoting aminoglycoside drug G418. Nonsense suppression was studied in the human cell lines 293 and MRC5V1 and the simian line COS-7. Overall, the rank order for the effect of changes to the base 3' to UAG was C lt G = U lt A. This study confirms and extends earlier findings that in mammalian cells 3' C supports efficient nonsense suppression while 3' A is unsympathetic for read-through at nonsense codons. The rules for the ***mammalian*** ***codon*** context effect on nonsense suppression are therefore demonstrably different from those in E. coli.

L15 ANSWER 18 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
14
AN 1995:298019 BIOSIS
DN PREV199598312319
TI Correlation between codon usage, regional genomic nucleotide composition, and amino acid composition in the cytochrome P-450 gene superfamily.
AU Porter, Todd D.
CS Div. Pharmacol. and Exp. Therapeutics, Coll. Pharmacy, Univ. Ky., Lexington, KY 40536-0082 USA
SO Biochimica et Biophysica Acta, (1995) Vol. 1261, No. 3, pp. 394-400.
ISSN: 0006-3002.
DT Article
LA English
AB The ***codon*** usage bias of 110 ***mammalian*** cytochrome P-450 genes has been determined and analyzed in relation to a variety of genetic, biochemical, and physiological parameters. In those P-450 genes exhibiting biased usage the preferred codons generally do not differ among the four species examined (rat, rabbit, man, and mouse) or from the predominantly used codons identified for all sequenced genes in a recent data base analysis (Wada et al. (1992) Nucleic Acids Res. 20 (Suppl.), 2111-2118). Codon usage bias does not correlate with evolutionary relationships, evolutionary age, or with the extent of evolutionary conservation of orthologous proteins; there is no obvious correlation with the level of expression of a given P-450, with its inducibility, nor with its physiologic role; and neither the preferred codons nor the degree of bias differ for P-450s expressed in different tissues. Codon usage bias does correlate with the C + G content at the codon third position, and thus preferred codons usually end in C or G; for those P-450s for which gene sequences are available this bias also correlates with the C + G content of the intronic and flanking regions of these genes. Moreover, a lesser increase in the C + G content at the codon first and second positions is also evident in genes located in regions of high C + G content; this leads to predictable differences in the amino acid compositions of P-450 enzymes that correlate with genomic nucleotide composition and the degree of bias in codon usage.

L15 ANSWER 19 OF 77 MEDLINE
AN 96342528 MEDLINE
DN 96342528 PubMed ID: 8746463
TI Identification of a glutathione peroxidase homolog in Neisseria meningitidis.
AU Aho E L; Kelly L P
CS Department of Biology, Concordia College, Moorhead, Minnesota, USA, 56562.
SO DNA SEQUENCE, ***(1995)*** 6 (1) 55-60.
Journal code: A9H; 9107800. ISSN: 1042-5179.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199612
ED Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961210
AB Glutathione peroxidase is an antioxidant enzyme found in a diverse array of eukaryotic species. We have determined the DNA sequence of a glutathione peroxidase homolog in the pathogenic bacterium Neisseria meningitidis. The sequence displays features of a functional gene, but lacks a selenocysteine-encoding in-frame TGA ***codon*** characteristic of most ***mammalian*** glutathione peroxidase genes. The derived amino acid sequence encoded by the N. meningitidis homolog predicts a 19.9 kDa protein that displays a high level of amino acid identity with other gluathione peroxidase sequences, particularly within four conserved regions of the enzyme.

L15 ANSWER 20 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
15
AN 1994:404071 BIOSIS
DN PREV199497417071
TI A thyroid hormone-regulated gene in Xenopus laevis encodes a type III iodothyronine 5-deiodinase.
AU St German, Donald L. (1); Schwartzman, Robert A.; Croteau, Walburga; Kanamori, Akira; Wang, Zhou; Brown, Donald D.; Galton, Valerie Anne
CS (1) Dep. Med. Physiol., Dartmouth Med. Sch., Lebanon, NH 03756 USA
SO Proceedings of the National Academy of Sciences of the United States of America, (1994) Vol. 91, No. 16, pp. 7767-7771.
ISSN: 0027-8424.
DT Article
LA English
AB The type III iodothyronine 5-deiodinase metabolizes thyroxine and

3,5,3'-triiodothyronine to inactive metabolites by catalyzing the removal of iodine from the inner ring. The enzyme is expressed in a tissue-specific pattern during particular stages of development in amphibia, birds, and mammals. Recently, a PCR-based subtractive hybridization technique has been used to isolate cDNAs prepared from Xenopus laevis tadpole tail mRNA that represent genes up-regulated by thyroid hormone during metamorphosis. Sequence analysis of one of these cDNAs (XL-15) revealed regions of homology to the mRNA encoding the rat type I (outer ring) 5'-deiodinase, including a conserved UGA ***codon*** that encodes selenocysteine in the ***mammalian*** enzyme. We report here that the protein encoded by the XL-15 cDNA efficiently catalyzes the (inner ring) 5-deiodination of 3,5,3'-triiodothyronine with a K-m value of 2 nM and is resistant to inhibition by propylthiouracil and aurothioglucose. Our analysis confirms that the UGA codon encodes a selenocysteine that is critical for the catalytic activity of the enzyme. In addition, the direct induction of XL- 15 mRNA levels by thyroid hormone in X. laevis tadpole tail tissue and cultured cell lines correlates closely with increases in 5- (but not 5'-) deiodinase activity. These findings indicate that the XL-15 cDNA encodes a type III 5-deiodinase and underscores the importance of the trace element selenium in thyroid hormone metabolism.

=> d bib abs 21-30

L15 ANSWER 21 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
16
AN 1994:531847 BIOSIS
DN PREV199497544847
TI Selenocysteine insertion or termination: Factors affecting UGA codon fate and complementary anticodon: Codon mutations.
AU Berry, Marla J. (1); Harney, John W.; Ohama, Takeshi; Hatfield, Dolph L.
CS (1) Thyroid Div., Brigham and Women's Hosp., Harvard Med. Sch., Boston, MA
02115 USA
SO Nucleic Acids Research, (1994) Vol. 22, No. 18, pp. 3753-3759.
ISSN: 0305-1048.
DT Article
LA English
AB Translation of UGA as selenocysteine instead of termination occurs in numerous proteins, and the process of recoding UGA requires specific signals in the corresponding mRNAs. In eukaryotes, stem - loops in the 3' untranslated region of the mRNAs confer this function. Despite the presence of these signals, selenocysteine incorporation is inefficient. To investigate the reason for this, we examined the effects of the amount of deiodinase cDNA on UGA read through in transfected cells, quantitating the full-length and UGA terminated products by Western blotting. The gene for the selenocysteine-specific tRNA was also cotransfected to determine if it was limiting. We find that the concentrations of both the selenoprotein DNA and the tRNA affect the ratio of selenocysteine incorporation to termination. Selenium depletion was also found to decrease read through. The fact that the truncated peptide is synthesized intracellularly demonstrates unequivocally that UGA can serve as both a stop and a selenocysteine codon in a single mRNA. Mutation of UGA to UAA (stop) or UUA (leucine) in the deiodinase mRNA abolishes deiodinase activity; but activity is partially restored when selenocysteine tRNAs containing complementary mutations are cotransfected. Thus, UGA is not essential for selenocysteine incorporation in ***mammalian*** cells, provided that ***codon*** :anticodon complementarity is maintained.

L15 ANSWER 22 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
17
AN 1994:449290 BIOSIS
DN PREV199497462290
TI Selection of silent sites in the rodent H3 histone gene family.
AU Debry, Ronald W. (1); Marzluff, William F.
CS (1) Dep. Bilogical Sci., Florida State Univ., Tallahassee, FL 32306-2043 USA
SO Genetics, (1994) Vol. 138, No. 1, pp. 191-202.
ISSN: 0016-6731.
DT Article
LA English
AB Selection promoting differential use of synonymous codons has been shown for several unicellular organisms and for Drosophila, but not for mammals. Selection coefficients operating on synonymous codons are likely to be extremely small, so that a very large effective population size is required for selection to overcome the effects of drift. In ***mammals*** , ***codon*** -usage bias is believed to be determined exclusively by mutation pressure, with differences between genes due to large-scale variation in base composition around the genome. The replication-dependent histone genes are expressed at extremely high levels during periods of DNA synthesis, and thus are among the most likely mammalian genes to be affected by selection on synonymous codon usage. We suggest that the extremely biased pattern of codon usage in the H3 genes is determined in part by selection. Silent site G + C content is much higher than expected based on flanking sequence G + C content, compared to other rodent genes with similar silent site base composition but lower levels of expression. Dinucleotide-mediated mutation bias does affect codon usage, but the affect is limited to the choice between G and C in some fourfold degenerate codons. Gene conversion between the two clusters of histone genes has not been an important force in the evolution of the H3 genes, but gene conversion appears to have had some effect within the cluster on chromosome 13.

L15 ANSWER 23 OF 77 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 94062666 EMBASE
DN 1994062666
TI Oligonucleotide probe for the detection of hereditary retinal degenerative diseases.
SO Current Opinion in Therapeutic Patents, (1994) 4/2 (169).
ISSN: 0962-2594 CODEN: COTPES
CY United Kingdom
DT Journal; (Short Survey)
FS 012 Ophthalmology
022 Human Genetics
030 Pharmacology
LA English
SL English
AB A probe which includes a purified single-stranded oligonucleotide, containing a region identical to the sequence of a six-nucleotide single-stranded segment of a gene encoding a mutant form of a human photoreceptor protein, is disclosed. The probe is useful for detecting a mutation in a gene encoding a human photoreceptor protein, or for diagnosing hereditary retinal disease (HRD) or a genetic predisposition to the disease. The term photoreceptor protein includes any protein which is expressed solely or predominantly by retinal cells. Where the photoreceptor protein is the protein encoded by the RDS gene, the mutation preferably includes a change in codon 219, 216, or 185, so that there is a change (such as a deletion at codon 219, a C-to-T transition in the second base of codon 216 or a T-to-C transition in the second base of ***codon*** 185). Transgenic non-human ***mammals*** are also disclosed some or all of whose nucleated cells contain a gene encoding a mutant form of a human photoreceptor protein. The animal models will provide a way to develop and test potential therapies for the various HRD diseases.

L15 ANSWER 24 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
18
AN 1994:126696 BIOSIS
DN PREV199497139696
TI DNA mismatch repair and synonymous ***codon*** evolution in ***mammals*** .
AU Eyre-Walker, Adam
CS Dep. Biol. Sci., Rutgers Univ., Piscataway, NJ 08855-1059 USA
SO Molecular Biology and Evolution, (1994) Vol. 11, No. 1, pp. 88-98.
ISSN: 0737-4038.
DT Article
LA English
AB It has been suggested that the differences in synonymous ***codon*** use between ***mammalian*** genes within a genome are due to differences in the efficiency of DNA mismatch repair. This hypothesis was tested by developing a model of mismatch repair, which was used to predict the expected relationship between the rate of substitution and G+C content at silent sites. It was found that the silent-substitution rate should decline with increasing G+C content over most of the G+C-content range, if it is assumed that mismatch repair is G+C biased, an assumption which is supported by data. This prediction was then tested on a set of 58 primate and artiodactyl genes. There was no evidence of a direct decline in substitution rate with increasing G+C content, for either twofold- or fourfold-degenerate sites. It was therefore concluded that variation in the efficiency of mismatch repair is not responsible for the differences in synonymous ***codon*** use between ***mammalian*** genes. In support of this conclusion, analysis of the model also showed that the parameter range over which mismatch repair can explain the differences in synonymous codon use between genes is very small.

L15 ANSWER 25 OF 77 MEDLINE
AN 94003397 MEDLINE
DN 94003397 PubMed ID: 8400357
TI ***Codon*** usage in ***mammalian*** genes is biased by sequence slippage mechanisms.
AU Bains W
CS PA Consulting Group, Melbourn, Royston, Herts, UK.
SO DNA SEQUENCE, ***(1993)*** 3 (5) 277-82.
Journal code: A9H; 9107800. ISSN: 1042-5179.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199311
ED Entered STN: 19940117
Last Updated on STN: 19940117
Entered Medline: 19931116
AB The codons for some conserved amino acids are found to be the same between
homologous genes from different species when the statistics of codon usage would suggest that they should be different. I examine whether this 'coincidence' of codon usage could be due to genetic mechanisms homogenising the DNA around specific sites. This paper describes the further analysis of the coincident codons in 19 genes (a total of 96 homologues) for slippage. Coincident codons arise in contexts of increased sequence simplicity, and have a high chance of occurring within sequences similar to the recombination-prone minisatellite 'core' sequence. This

suggests a role of genetic homogenisation in their generation.

L15 ANSWER 26 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
19
AN 1992:257580 BIOSIS
DN BA93:133905
TI SPECIFIC PROTEIN BINDING TO A CONSERVED REGION OF THE ORNITHINE
DECARBOXYLASE MRNA 5'-UNTRANSLATED REGION.
AU MANZELLA J M; BLACKSHEAR P J
CS BOX 3897, DUKE UNIVERSITY MEDICAL CENTER, DURHAM, N.C. 27710.
SO J BIOL CHEM, (1992) 267 (10), 7077-7082.
CODEN: JBCHA3. ISSN: 0021-9258.
FS BA; OLD
LA English
AB An RNA gel retardation assay was used to identify one or more cellular protein(s) (ornithine decarboxylase mRNA 5'-UTR binding protein (ODCBP)) that bind specifically to a conserved region of the 5'-untranslated region (5'-UTR) of rat ornithine decarboxylase (ODC) mRNA. Ultraviolet light cross-linking demonstrated that this protein has an apparent Mr = 58,000 in mammalian cells. Treatment with the oxidizing agent diamide prevented binding of the ODCBP to ODC mRNA; addition of .beta.-mercaptoethanol reversed this inhibition and permitted mRNA.cntdot.ODCBP complex formation. Cytoplasmic extracts from a variety of animal cells and tissues demonstrated similar binding activities; however, there was marked tissue-specific expression of the protein in the rat, with brain, heart, lung, and testis containing large amounts, and kidney, spleen, and skeletal muscle expressing negligible amounts. Binding was completely prevented by several mutations within a highly conserved heptanucleotide region (CCAU/ACUC) that was within 61 bases of the initiation ***codon*** in ODC mRNAs from ***mammals*** , Xenopus and Caenorhabditis elegans; mutations 5' and 3' of the conserved heptanucleotide domain had no effect on binding activity. Binding was not affected by manipulation of cellular polyamine levels or by treatment of cells with agents that stimulate ODC biosynthesis. Thus, we have identified a widely distributed cellular protein that binds to a conserved domain within the 5'-UTR of ODC mRNA from many animal species; functional consequences of this binding remain to be determined.

L15 ANSWER 27 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1992:389956 BIOSIS
DN BA94:62131
TI CONTROL OF TRANSLATION INITIATION IN SACCHAROMYCES-CEREVISIAE.
AU YOON H; DONAHUE T F
CS DEP. BIOL., INDIANA UNIV., BLOOMINGTON, INDIANA 47405, USA.
SO MOL MICROBIOL, (1992) 6 (11), 1413-1419.
CODEN: MOMIEE. ISSN: 0950-382X.
FS BA; OLD
LA English
AB The first observations regarding the control of translation initiation in the yeast Saccharomyces cerevisiae were made by Fred Sherman and his colleagues in 1971. Elegant genetic studies of the CYC1 gene resulted in the formulation of 'Sherman's Rules' for translation initiation as follows: (i) AUG is the only initiator codon. (ii) the most proximal AUG from the 5' end of a message will serve as the start site of translation; and (iii) if the upstream codon is mutated then initiation begins at the next available AUG in the message. Hidden within these rules is the mechanism of eukaryotic translation initiation, as these very same rules were later shown to apply to higher eukaryotic organisms and were formulated into the scanning model. However, only in the past five years has yeast been taken seriously as an organism for studying the mechanism of eukaryotic translation initiation. The basis for this is that the yeast genes for at least four mammalian translation initiation factor homologues have been identified and the number is growing. Similar factors suggest similar mechanisms for translation initiation between yeast and mammals. For some translation initiation factors, the genetics of yeast has provided new insights into their function. A mechanism for regulating translation initiation in mammalian cells is now evident in yeast. It seems clear that the molecular genetics of yeast coupled with the available in vitro translation system will provide a wealth of information in the future regarding translational control and regulatory mechanisms. The purpose of ths review is to summarize what is known about translational control in S. cerevisiae.

L15 ANSWER 28 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
20
AN 1993:50315 BIOSIS
DN PREV199395026617
TI Conservation of the mammalian RNA polymerase II largest-subunit C-terminal domain.
AU Barron-Casella, Emily; Corden, Jeffry L. (1)
CS (1) Dep. Pediatr. Hematol., Johns Hopkins Univ. Sch. Med., 725 N. Wolfe St., Baltimore, Md. 21205
SO Journal of Molecular Evolution, (1992) Vol. 35, No. 5, pp. 405-410. ISSN: 0022-2844.
DT Article
LA English
AB We have isolated and sequenced a portion of the gene encoding the carboxy-terminal domain (CTD) of the largest subunit of RNA polymerase II from three mammals. These mammalian sequences include one rodent and two primate CTDs. Comparisons of the new sequences to mouse and Chinese hamster show a high degree of conservation among the ***mammalian*** CTDs. Due to synonymous ***codon*** usage, the nucleotide differences between hamster, rat, ape, and human result in no amino acid changes. The amino acid sequence for the mouse CTD appears to have one different amino acid when compared to the other four sequences. Therefore, except for the one variation in mouse, all of the known mammalian CTDs have identical amino acid sequences. This is in marked contrast to the situation among more divergent species. The present study suggests that there is a strong evolutionary pressure to maintain the primary structure of the mammalian CTD.

L15 ANSWER 29 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1992:469574 BIOSIS
DN BR43:90924
TI SITE-DIRECTED MUTAGENESIS OF SEROTONIN 5-HT-2 RECEPTORS.
AU SHIH J C; GALLAHER T; WANG C-D; CHEN K
CS DEP. MOL. PHARMACOL. TOXICOL., UNIV. SOUTHERN CALIF., SCH. PHARM., LOS
ANGELES, CALIF. 90033.
SO MEETING OF THE SOCIETY FOR NEUROSCIENCE ON RECENT ADVANCES IN SEROTONIN
RESEARCH II: POLYMERASE CHAIN REACTION TO POSITRON EMISSION TOMOGRAPHY,
NEW ORLEANS, LOUISIANA, USA. J CHEM NEUROANAT. (1992) 5 (4), 281-282.
CODEN: JCNAEE. ISSN: 0891-0618.
DT Conference
FS BR; OLD
LA English

L15 ANSWER 30 OF 77 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
21
AN 1992:523470 BIOSIS
DN BA94:131545
TI FOUR SYNONYMOUS GENES ENCODE CALMODULIN IN THE TELEOST FISH MEDAKA
ORYZIAS-LATIPES CONSERVATION OF THE MULTIGENE ONE-PROTEIN PRINCIPLE.
AU MATSUO K; SATO K; IKESHIMA H; SHIMODA K; TAKANO T
CS DEP. MICROBIOLOGY, KEIO UNIVERSITY SCHOOL MEDICINE, 35 SHINANOMACHI,
SHINJUKU-KU, TOKYO 160, JPN.
SO GENE (AMST), (1992) 119 (2), 279-281.
CODEN: GENED6. ISSN: 0378-1119.
FS BA; OLD
LA English
AB We cloned four distinct calmodulin (CaM)-encoding cDNAs from a small teleost fish, medaka (Oryzias latipes). The deduced amino acid (aa) sequences were exactly the same in these four genes and identical to the aa sequence of ***mammalian*** CaM, because of synonymous ***codon*** usages. The four cDNAs from medaka, termed CaM-A, -B, -C and
-D, corresponded to mRNAs of 1.8, 1.4, 2.5 and 1.8 kb, respectively, in Northern blot analysis. Our results demonstrated that the 'multigene one-protein' principle of CaM synthesis is applicable to medaka, as well as to mammals whose CaM is encoded by at least three different genes.

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NEWS 7 Mar 22 TOXLIT no longer available
NEWS 8 Mar 22 TRCTHERMO no longer available
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NEWS 17 Apr 22 BIOSIS Gene Names now available in TOXCENTER
NEWS 18 Apr 22 Federal Research in Progress (FEDRIP) now available

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L3 ANSWER 1 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:43541 BIOSIS
DN PREV199900043541
TI Exploring the role of FGF signaling in CNS progenitor cells using a ***Cre*** /lox ***transgenic*** ***mouse*** system.
AU Hebert, Jean M.; McConnell, Susan K.
SO Society for Neuroscience Abstracts, (1998) Vol. 24, No. 1-2, pp. 281. Meeting Info.: 28th Annual Meeting of the Society for Neuroscience, Part 1 Los Angeles, California, USA November 7-12, 1998 Society for Neuroscience . ISSN: 0190-5295.
DT Conference
LA English

L3 ANSWER 2 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:1323 BIOSIS
DN PREV199900001323
TI Transgenic Cre recombinase expression in germ cells and early embryogenesis directs homogeneous and ubiquitous deletion of loxP-flanked gene segments.
AU Bergqvist, Ingela; Eriksson, Bjorn; Eriksson, Maria; Holmberg, Dan (1)
CS (1) Dep. Cell and Mol. Biol., Umea Univ., S-901 87 Umea Sweden
SO FEBS Letters, (***Oct. 30, 1998***) Vol. 438, No. 1-2, pp. 76-80. ISSN: 0014-5793.
DT Article
LA English
AB We report on the establishment of a ***transgenic*** ***mouse*** line expressing ***Cre*** recombinase under control of the c-kit promoter. Expression of Cre recombinase was only observed in late spermatogenesis and oogenesis, however, Cre-mediated deletion of floxed gene segments occurred at this stage as well as in early embryogenesis. As a consequence of this, a chimeric distribution of loxed alleles was found in a large fraction of these mice. The chimerism was very homogeneous in different organs and tissues of the same individual but varied between different individual offspring. The potential uses for this mouse line are discussed.

L3 ANSWER 3 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:289789 BIOSIS
DN PREV199800289789
TI Generation of a tissue specific ***transgenic*** ***mouse*** model using ***CRE*** recombinase linked to an insulin promoter.
AU Ray, M. K. (1); Demayo, F. J.; Brunicardi, F. C.
CS (1) Dep. Surg., Baylor Coll. Med., Houston, TX USA
SO Gastroenterology, (***April 15, 1998***) Vol. 114, No. 4 PART 2, pp. A1418-A1419.
Meeting Info.: Digestive Diseases Week and the 99th Annual Meeting of the American Gastroenterological Association New Orleans, Louisiana, USA May 16-22, 1998 American Association for the Study of Liver Diseases . ISSN: 0016-5085.
DT Conference
LA English

L3 ANSWER 4 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:120891 BIOSIS
DN PREV199800120891
TI Microinjection of Cre recombinase RNA induces site-specific recombination of a transgene in mouse oocytes.
AU de Wit, Ton; Drabek, Dubravka; Grosveld, Frank (1)
CS (1) Erasmus Univ. Rotterdam, MGC-Dep. Cell Biol., P.O. Box 1738, 3000 DR Rotterdam Netherlands
SO Nucleic Acids Research, (***Jan. 15, 1998***) Vol. 26, No. 2, pp. 676-678.
ISSN: 0305-1048.
DT Article
LA English
AB We have developed a strategy for producing single copy ***transgenic*** ***mouse*** lines using ***Cre*** -loxP site specific recombination. The method is based on transient expression of the recombinase after injection of in vitro transcribed mRNA into the cytoplasm of fertilised eggs containing multiple copies of the transgene. The success rate of the recombination event is 100% (15 out of 15).

L3 ANSWER 5 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:514554 BIOSIS
DN PREV199799813757
TI Generation of Cre recombinase-specific monoclonal antibodies, able to characterize the pattern of ***Cre*** expression in ***cre*** - ***transgenic*** ***mouse*** strains.
AU Schwenk, Frieder (1); Sauer, Brian; Kukoc, Natasa; Hoess, Ronald; Mueller, Werner; Kocks, Christine; Kuehn, Ralf; Rajewsky, Klaus
CS (1) Inst. Genetics, Univ. Cologne, Weyertal 121, D-50931 Cologne Germany
SO Journal of Immunological Methods, (1997) Vol. 207, No. 2, pp. 203-212. ISSN: 0022-1759.
DT Article
LA English
AB Transgene-encoded Cre recombinase can target alteration of loxP-tagged genes to specific cell types and developmental stages in mice, depending on the pattern of transgene expression. To facilitate determination of the latter, we have generated monoclonal anti-Cre antibodies which are specific for distinct epitopes on the recombinase and detect Cre both on immunoblots and intracellularly by immunofluorescence. We demonstrate the usefulness of these antibodies by an analysis of Cre expression in mice carrying a cre-transgene under B cell-specific control.

L3 ANSWER 6 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:438491 BIOSIS
DN PREV199799737694
TI A ***transgenic*** ***mouse*** line that retains ***Cre*** recombinase activity in mature oocytes irrespective of the cre transgene transmission.

AU Sakai, Katsunaga; Miyazaki., Juni-Ichi (1)
CS (1) Dep. Nutr. Physiol. Chem., Osaka Univ. Med. Sch., 2-2 Yamadaoka, Suita, Osaka 565 Japan
SO Biochemical and Biophysical Research Communications, (1997) Vol. 237, No. 2, pp. 318-324.
ISSN: 0006-291X.
DT Article
LA English
AB The Cre/loxP site-specific recombination system derived from bacteriophage P1 provides a convenient tool for directed modifications of genomes in various organisms. To exploit Cre-mediated manipulation of mouse genomic sequences at the zygote stage, we have developed a transgenic mouse line carrying the CAGcre transgene in which the ere gene is under control of the cytomegalovirus immediate early enhancer-chicken beta-actin hybrid (CAG) promoter. The activity of the Cre recombinase at early stages of development was examined by crossing the CAG-cre transgenic mice to another transgenic mouse line carrying a reporter gene construct, CAG-CAT-Z, which directs expression of the E. coli lacZ gene upon Cre-mediated excision of the loxP-flanked chloramphenicol acetyltransferase (CAT) gene located between the CAG promoter and the lacZ gene. PCR-based analysis of F1 progeny from CAG-cre males x CAG-CAT-Z females showed that transmission of the CAG-cre transgene was accompanied by the complete deletion of the CAT gene of the CAG-CAT-Z transgene in all tissues, and that this deletion was never observed in the progeny without transmission of the CAG-cre gene. On the other hand, analysis of F1 mice from CAG-CAT-Z males x CAG-cre females showed that the CAG-CAT-Z transgene had undergone complete deletion of the CAT gene in all tissues irrespective of the cotransmission of the CAG-cre gene. This Cre-mediated recombination in F1 mice occurred before the two-cell stage of embryonic development, as shown by X-gal staining. The results suggest that the CAG-cre transgene is expressed in developing oocytes of CAG-cre transgenic mice, and Cre mRNA and/or protein are retained in mature oocytes irrespective of the transmission of the CAG-cre transgene, resulting in efficient Cre-mediated recombination of paternally derived target genes upon fertilization. The CAG- ***cre*** ***transgenic*** ***mouse*** should serve as a useful tool to introduce prescribed genetic modifications into the mouse embryo at the zygote stage.

L3 ANSWER 7 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:156061 BIOSIS
DN PREV199799455264
TI Zp3- ***cre*** , a ***transgenic*** ***mouse*** line for the activation or inactivation of loxP-flanked target genes specifically in the female germ line.
AU Lewandoski, Mark; Wassarman, Karen Montzka; Martin, Gail R. (1)
CS (1) Dep. Anat. Program Developmental Biol., Sch. Med., Univ. California, San Francisco, CA 94143-0452 USA
SO Current Biology, (1997) Vol. 7, No. 2, pp. 148-151.
ISSN: 0960-9822.
DT Article
LA English
AB The site-specific DNA recombinase Cre is being used to develop a now generation of tools for controlling gene expression in mice. Cre mediates the recombination of two directly repeated target (loxP) sites to a single loxP site, with concomitant excision of the DNA segment flanked by the loxP sites (the 'floxed' DNA). Such recombination can function to activate a gone by excising a floxed DNA segment that blocks expression because it either separates the regulatory and coding sequences of the gene or interrupts the gene's open reading frame. Conversely, DNA excision can inactivate a gene if an essential fragment of the gone is floxed. Gene activation or inactivation in vivo can be achieved by mating two different animals, one carrying a 'target gene' with appropriately placed loxP sites and one carrying a cre transgene. In most cases, the specificity of the system is dependent upon stringent regulation of cre expression. We describe here a mouse line in which cre expression is controlled by regulatory sequences from the mouse zona pellucida 3 (Zp3) gene, which Ls normally expressed exclusively in the growing oocyte prior to the completion of the first meiotic division. We show that in target-bearing Zp3-cre mice, Cre-mediated recombination of the target gene apparently occurs in 100% of oocytes. Moreover, Cre activity is not detected in the somatic tissues of most target-bearing Zp3-cre mice. Potential uses for this mouse line are discussed.

L3 ANSWER 8 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:537570 BIOSIS
DN PREV199699259926
TI Sustained somatic gene inactivation by viral transfer of Cre recombinase.
AU Rohlmann, Astrid; Gotthardt, Michael; Willnow, Thomas E.; Hammer, Robert E.; Herz, Joachim (1)
CS (1) Dep. Mol. Genet., Howard Hughes Med. Inst., Univ. Texas Southwestern Med. Cent., Dallas, TX 75235 USA
SO Nature Biotechnology, (1996) Vol. 14, No. 11, pp. 1562-1565.
ISSN: 1087-0156.
DT Article
LA English
AB Transgenic and knockout mice have proven invaluable tools for analyzing physiologically relevant functions of numerous genes. In some cases, however, pleiotropic effects that result from a variable requirement for a particular gene in different tissues, cell types, or stages of embryonic development may complicate the analysis due to a complex phenotype or embryonic lethality. The loxP/Cre-mediated recombination system, which allows tissue-specific gene targeting in the mouse, can be used to overcome these problems. A limitation of current methods is that a mouse carrying a loxP-tagged gene must be crossed with a ***transgenic*** ***mouse*** expressing the ***Cre*** recombinase in an appropriate tissue to obtain the desired gene rearrangement. We have used recombinant adenovirus carrying the Cre recombinase to induce virtually quantitative somatic cell gene disruption in the liver, The targeted gene was the multifunctional low-density lipoprotein receptor-related protein (LRP), a cell surface receptor for alpha-2-macroglobulin and other ligands. Transient expression of Cre following adenoviral infection produced the predicted gene rearrangement, functionally inactivating LRP in the liver. Rearrangement occurred within 6 days after infection and remained stable for at least 28 days. The results demonstrate the suitability of adenoviral Cre gene transfer to induce long-term, quantitative, and temporally controlled gene disruption in the mouse.

L3 ANSWER 9 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:537543 BIOSIS
DN PREV199699259899
TI Bypass of lethality with mosaic mice generated by Cre-loxP-mediated recombination.
AU Betz, Ulrich A. K. (1); Vosshenrich, Christian A. J.; Rajewsky, Klaus; Mueller, Werner
CS (1) Inst. Gen., Univ. Cologne, Weyertal 121, D-50931 Cologne Germany
SO Current Biology, (1996) Vol. 6, No. 10, pp. 1307-1316.
ISSN: 0960-9822.
DT Article
LA English
AB Background: The analysis of gene function based on the generation of mutant mice by homologous recombination in embryonic stem cells is limited if gene disruption results in embryonic lethality. Mosaic mice, which contain a certain proportion of mutant cells in all organs, allow lethality to be circumvented and the potential of mutant cells to contribute to different cell lineages to be analyzed. To generate mosaic animals, we used the bacteriophage P1 -derived Cre-/oxP recombination system, which allows gene alteration by Cre-mediated deletion of loxP-flanked gene segments. Results: We generated nesting- ***cre*** ***transgenic*** ***mouse*** lines, which expressed the Cre recombinase under the control of the rat nesting promoter and its second intron enhancer. In crosses to animals carrying a loxP-flanked target gene, partial deletion of the loxP-flanked allele occurred before day 10.5 post coitum and was detectable in all adult organs examined, including germ-line cells. Using this approach, we generated mosaic mice containing cells deficient in the gamma-chain of the interleukin-2 receptor (IL-2R-gamma); in these animals, the IL-2R-gamma-deficient cells were underrepresented in the thymus and spleen. Because mice deficient in DNA polymerase beta die perinatally, we studied the effects of DNA polymerase beta deficiency in mosiac animals. We found that some of the mosaic polymerase beta-deficient animals were viable, but were often reduced in size and weight. The fraction of DNA polymerase beta-deficient cells in mosaic embryos decreased during embryonic development, presumably because wild-type cells had a competitive advantage. Conclusions: The nesting-cre transgenic mice can be used to generate mosaic animals in which target genes are mutated by Cre-mediated recombination of loxP-flanked target genes. By using mosaic animals, embryonic lethality can be bypassed and cell lineages for whose development a given target gene is critical can be identified. In the case of DNA polymerase beta, deficient cells are already selected against during embryonic development, demonstrating the general importance of this protein in multiple cell types.

L3 ANSWER 10 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:332298 BIOSIS
DN PREV199699054654
TI Efficient in vivo manipulation of mouse genomic sequences at the zygote stage.
AU Lakso, Merja; Pichel, Jose G.; Gorman, James R.; Sauer, Brian; Okamoto, Yo; Lee, Eric; Alt, Frederick W.; Westphal, Heiner (1)
CS (1) Natl. Inst. Health, Build. 6B, Room 413, 6 Center Dr., Bethesda, MD 20892-2790 USA
SO Proceedings of the National Academy of Sciences of the United States of America, (1996) Vol. 93, No. 12, pp. 5860-5865.
ISSN: 0027-8424.
DT Article
LA English
AB We describe a ***transgenic*** ***mouse*** line carrying the ***cre*** transgene under the control of the adenovirus Ella promoter that targets expression of the Cre recombinase to the early mouse embryo. To assess the ability of this recombinase to excise loxP-flanked DNA sequences at early stages of development, we bred Ella-cre transgenic mice to two different mouse lines carrying loxP-flanked target sequences: (i) a strain with a single gene-targeted neomycin resistance gene flanked by loxP sites and (ii) a transgenic line carrying multiple transgene copies with internal loxP sites. Mating either of these loxP-carrying mouse lines to Ella-cre mice resulted in first generation progeny in which the loxP-flanked sequences had been efficiently deleted from all tissues tested, including the germ cells. Interbreeding of these first generation progeny resulted in efficient germ-line transmission of the deletion to subsequent generations. These results demonstrate a method by which loxP-flanked DNA sequences can be efficiently deleted in the early mouse

embryo. Potential applications of this approach are discussed, including reduction of multicopy transgene loci to produce single-copy transgenic lines and introduction of a variety of subtle mutations into the germ line.

L3 ANSWER 11 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:107081 BIOSIS
DN PREV199698679216
TI A ***cre*** - ***transgenic*** ***mouse*** strain for the ubiquitous deletion of loxP-flanked gene segments including deletion in germ cells.
AU Schwenk, Frieder (1); Baron, Udo; Rajewsky, Klaus
CS (1) Inst. Genetics, Univ. Cologne, Weyertal 121, 50931 Cologne Germany
SO Nucleic Acids Research, (1995) Vol. 23, No. 24, pp. 5080-5081. ISSN: 0305-1048.
DT Article
LA English

L3 ANSWER 12 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1993:4291 BIOSIS
DN PREV199395004291
TI The identification of a cis-acting element involved in cyclic-3',5'-adenosine monophosphate regulation of bovine vasopressin gene expression.
AU Pardy, Karen; Adan, Roger A. H.; Carter, David A.; Seah, Valerie; Burbach, J. Peter H.; Murphy, David (1)
CS (1) Neuropeptide Laboratory, Institute Molecular Cell Biology, National University Singapore, Singapore 0511 Singapore
SO Journal of Biological Chemistry, (1992) Vol. 267, No. 30, pp. 21746-21752. ISSN: 0021-9258.
DT Article
LA English
AB Cyclic adenosine 3',5'-monophosphate (cAMP) has been implicated as an intracellular messenger mediating osmotic regulation of expression of the gene encoding the neuropeptide vasopressin (VP) in the hypothalamus. We have used a heterologous transient transfection system to demonstrate that cAMP regulates the bovine VP gene promoter following transfection into CV1 cells. Mutational analysis identified a bovine VP cAMP-responsive element (BVP-CRE) 120-112 base-pairs upstream of the start of transcription. DNase I footprint analysis using nuclear protein extract from CV1 cells showed protection at the site of the BVP-CRE. Protection of the BVP-CRE was also observed using purified AP1 protein, while there was a weak interaction with the BVP-CRE using purified rat CREB protein. Nuclear proteins purified from the rat supraoptic nucleus bind to the BVP- ***CRE*** . As ***transgenic*** ***mouse*** studies have shown that the bovine VP gene is subject to appropriate physiological regulation in the mouse hypothalamus (Ang, H. L., Funkhouser, J., Carter, D. A., Ho, M. Y., and Murphy, D. (1991) Soc. Neurosci. Abstr. 513, 12), these data indicate a role for the BVP-CRE element in mediating VP gene expression in vivo. These data demonstrate that cAMP regulates bovine VP gene expression in vitro via a cis-acting element within the VP promoter, and this activation may be mediated by members of the AP1/ATF/CREB family of transcription factors.

L3 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2002 ACS
AN 1998:810202 CAPLUS
DN 130:134907
TI A mouse model for beta cell-specific ablation of target gene(s) using the Cre-loxP system
AU Ray, M. K.; Fagan, S. P.; Moldovan, S.; DeMayo, F. J.; Brunicardi, F. C.
CS Department of Surgery, Baylor College of Medicine, Houston, TX, 77030, USA
SO Biochemical and Biophysical Research Communications (***1998***), 253(1), 65-69
CODEN: BBRCA9; ISSN: 0006-291X
PB Academic Press
DT Journal
LA English
AB The rat insulin promoter (RIP) has been used to drive the expression of Cre recombinase (Cre) specifically in beta cells. Transient transfection was performed in the mouse insulinoma cell line, NIT-1, and control cell lines. RT-PCR was performed using total RNA from pancreas and other tissues of RIP-Cre transgenic mice. In addn., the efficiency and specificity of RIP were further analyzed by cross breeding the RIP-Cre transgenic mice with reporter mice bearing a .beta.-actin-loxP-CAT-loxP-lacZ transgene. In these mice, lacZ is expressed only after excision of the floxed-CAT gene by Cre-mediated recombination. Here, we present the data for beta cell-specific expression of lacZ in bigenic mice, as proof of concept in a mouse model for targeting beta cell-specific gene(s). The RIP-Cre transgenic mice will be used as a potential tool for targeting the excision of beta cell-specific gene(s) to study their role in islet cell physiol. (c) 1998 Academic Press.
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2002 ACS
AN 1998:630111 CAPLUS
DN 130:948
TI Cre expression in primary spermatocytes: a tool for genetic engineering of the germ line
AU Vidal, Frederique; Sage, Julien; Cuzin, Francois; Rassoulzadegan, Minoo
CS Unite 470 de l'Institut National de la Sante et de la Recherche Medicale, Universite de Nice, Fr.
SO Molecular Reproduction and Development (***1998***), 51(3), 274-280
CODEN: MREDEE; ISSN: 1040-452X
PB Wiley-Liss, Inc.
DT Journal
LA English
AB Transgenic mice were generated expressing a testicular Cre recombinase driven by promoter sequences derived from the gene encoding Synaptonemal Complex Protein 1 (Sycp1), expressed at an early stage of the male meiosis (leptotene to zygotene). Recombination at target LoxP sites was examd. during germinal differentiation in mice harboring Sycp1-Cre and a second transgene where LoxP sites flank either the .beta.geo coding region, the Pgk1 promoter, or a tk-neo cassette inserted into the Rxr.alpha. locus. The LoxP-flanked transgenes were stably maintained in the somatic tissues of the double transgenic animals, as well as in the progeny of the females. Mice born after mating the double-transgenic males with normal females showed extensive deletions of the LoxP-flanked sequences. When the males were hemizygous for the Sycp1-Cre transgene, the deletions were obsd. even in the fraction of the offspring which had not inherited the Cre gene, thus demonstrating that expression occurred in the male parent during spermatogenesis. The high efficiency of excision at the LoxP sites makes the Sycp1-Cre transgenic males suitable for evaluating the role of defined gene functions in the germinal differentiation process.
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2002 ACS
AN 1998:571691 CAPLUS
DN 129:326684
TI Reporter gene activation in transgenic mice mediated through induced Cre/loxP recombination
AU Ayral, Anne-Marie; Kolossov, Evgueni; Serwe, Matthias; Sablitzky, Fred
CS Max-Delbuck-Laboratorium in der Max-Planck-Gesellschaft, Koln, 50829, Germany
SO Transgenics (***1998***), 2(3), 225-231
CODEN: TADTEF; ISSN: 1023-6171
PB Harwood Academic Publishers
DT Journal
LA English
AB The site-specific recombinase Cre can be employed in transgenic mice to activate or inactivate genes in a lineage specific way. This elegant approach to switch genes on or off in specific cell-types in vivo is dependent upon a tightly regulated expression of the Cre recombinase. More recently it was demonstrated that genes can be inactivated upon induced Cre-mediated recombination in many tissues of the mouse. In order to assess the feasibility to switch on genes in an inducible fashion, utilising the Cre/loxP recombination system, we established an indicator mouse line carrying a .beta.-galactosidase (lacZ) gene as a transgenic reporter. The expression of the lacZ gene is dependent upon a Cre/loxP-mediated deletion of a transcriptional stop signal situated between the Polyoma-enhancer/thymidine-kinase promoter and the lacZ gene. We demonstrate here that expression of the lacZ gene is activated upon induced Cre-mediated recombination in double transgenic animals. The Cre/loxP recombination system can thus be used to activate transgenes in a temporally regulated fashion. Furthermore, the indicator mouse line might serve as a tool to assess and confirm the spatially and/or temporally controlled Cre expression in transgenic mice.

L3 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2002 ACS
AN 1997:765930 CAPLUS
DN 128:85074
TI Cre-mediated gene deletion in the mammary gland
AU Wagner, Kay-Uwe; Wall, Robert J.; St-Onge, Luc; Gruss, Peter; Wynshaw-Boris, Anthony; Garrett, Lisa; Li, Minglin; Furth, Priscilla A.; Hennighausen, Lothar
CS Laboratory of Metabolism and Biochemistry, National Institute of Diabetes Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892, USA
SO Nucleic Acids Res. (***1997***), 25(21), 4323-4330
CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB To delete genes specifically from mammary tissue using the Cre-lox system, we have established transgenic mice expressing Cre recombinase under control of the WAP gene promoter and the MMTV LTR. Cre activity in these mice was evaluated by three criteria. First, the tissue distribution of Cre mRNA was analyzed. Second, an adenovirus carrying a reporter gene was used to det. expression at the level of single cells. Third, tissue specificity of Cre activity was detd. in a mouse strain carrying a reporter gene. In adult MMTV-Cre mice expression of the transgene was confined to striated ductal cells of the salivary gland and mammary epithelial cells in virgin and lactating mice. Expression of WAP-Cre was only detected in alveolar epithelial cells of mammary tissue during lactation. Anal. of transgenic mice carrying both the MMTV-Cre and the reporter transgenes revealed recombination in every tissue. In contrast, recombination mediated by Cre under control of the WAP gene promoter was largely restricted to the mammary gland but occasionally obsd. in the brain. These results show that transgenic mice with WAP-Cre but not MMTV-Cre can be used as a powerful tool to study gene function in development and tumorigenesis in the mammary gland.

L3 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2002 ACS
AN 1996:622324 CAPLUS
DN 125:266875
TI Temporal control of the Cre recombinase in transgenic mice by a tetracycline responsive promoter
AU St-Onge, Luc; Furth, Priscilla A.; Gruss, Peter
CS Dep. Molecular Cell Bio., Max-Planck-Inst. Biophys. Chem., Goettingen, 37018, Germany
SO Nucleic Acids Res. (***1996***), 24(19), 3875-3877
CODEN: NARHAD; ISSN: 0305-1048
DT Journal
LA English
AB Gene-targeted mice derived from embryonic stem cells are a useful tool to study gene function during development. However, if the mutation is embryonic lethal and the gene is deleted from the onset of development, later functions in adult animals cannot be studied. Recently, the bacterial Cre-loxP site-specific recombination system has successfully been used in transgenic animals to produce tissue-specific and temporal deletions [Tu et al. (1993) Cell, 73, 1155-1164; Gu et al. (1994) Science, 265, 103-106; Kuehn et al. (1995) Science, 269, 14237-1429]. We have evaluated the tetracycline responsive binary system [Gossen and Bujard (1992) Proc. Natl. Acad. Sci. USA, 89, 5547-5551] for its ability to transiently express the Cre recombinase in transgenic mice. In this system, a transactivator fusion protein composed of the tetracycline repressor (tetR) and the acidic domain of the herpes simplex viral protein 16 (VP16) can regulate the expression of the Cre gene from a promoter contg. tet-operator (tetO) sequences. In the absence of tetracycline, the Cre gene is expressed and will induce site-specific recombination between two loxP sites. In the presence of tetracycline, the Cre gene will not be expressed and recombination will not occur.

L3 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS
AN 1995:303142 CAPLUS
DN 122:152327
TI Conditional gene targeting. New strategy for targeted mutagenesis in mice
AU Shibata, Hiroyuki; Noda, Tetsuo
CS Dep. Cell Biol., Cancer Inst., Tokyo, 170, Japan
SO Jikken Igaku (***1995***), 13(1), 73-6
CODEN: JIIGEF; ISSN: 0288-5514
DT Journal; General Review
LA Japanese
AB A review, with 6 refs., on necessity of conditional gene targeting that has a regulating system for inactivation of a target gene, use of site-specific recombinase for time- or tissue-specific regulation of gene targeting, and prepn. of a conditional gene targeting mouse by hybridizing a ***transgenic*** ***mouse*** capable of expressing ***Cre*** (site-specific recombinase of bacteriophage P1) and a targeting mouse having 2 loxP (recognition sequence of Cre) sequences within the target gene followed by induction of Cre by a inducer.

L3 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2002 ACS
AN 1992:544525 CAPLUS
DN 117:144525
TI Tissue- and site-specific DNA recombination in transgenic mice
AU Orban, Paul C.; Chui, Daniel; Marth, Jamey D.
CS Biomed. Res. Cent., Univ. British Columbia, Vancouver, BC, V6T 1Z3, Can.
SO Proc. Natl. Acad. Sci. U. S. A. (***1992***), 89(15), 6861-5
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB A method of specifically modifying the mammalian genome in vivo was developed. This procedure comprises heritable tissue-specific and site-specific DNA recombination as a function of recombinase expression in transgenic mice. Transgenes encoding the bacteriophage P1 Cre recombinase and the loxP-flanked .beta.-galactosidase gene were used to generate transgenic mice. Genomic DNA from doubly transgenic mice exhibited tissue-specific DNA recombination as a result of Cre expression. Further characterization revealed that this process was highly efficient at distinct chromosomal integration sites. These studies also imply that Cre-mediated recombination provides a heritable marker for mitoses following the loss of Cre expression. This transgene-recombination system permits unique approaches to in vivo studies of gene function within exptl. defined spatial and temporal boundaries.

L3 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2002 ACS
AN 1992:505280 CAPLUS
DN 117:105280
TI Targeted oncogene activation by site-specific recombination in transgenic mice
AU Lakso, M.; Sauer, B.; Mosinger, B., Jr.; Lee, E. J.; Manning, R. W.; Yu, S. H.; Mulder, K. L.; Westphal, H.
CS Natl. Inst. Child Health Hum. Dev., Natl. Inst. Health, Bethesda, MD, 20892, USA
SO Proc. Natl. Acad. Sci. U. S. A. (***1992***), 89(14), 6232-6
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB An efficient and accurate method for controlled in vivo transgene modulation by site-directed recombination is described. Seven transgenic mouse founder lines were produced carrying the murine lens-specific .alpha.A-crystallin promoter and the simian virus 40 large tumor-antigen gene sequence, sepd. by a 1.3-kilobase-pair Stop sequence that contains elements preventing expression of the large tumor-antigen gene and Cre recombinase recognition sites. Progeny from two of these lines were mated with transgenic mice expressing the Cre recombinase under control of either the murine .alpha.A-crystallin promoter or the human cytomegalovirus promoter. All double-transgenic offspring developed lens tumors. Subsequent anal. confirmed that tumor formation resulted from large tumor-antigen activation via site-specific, Cre-mediated deletion of Stop sequences.

=> d his

(FILE 'HOME' ENTERED AT 20:33:29 ON 08 MAY 2002)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 20:33:39 ON 08 MAY 2002
L1 99 S CRE (3A) TRANSGEN? MOUSE
L2 56 DUP REM L1 (43 DUPLICATES REMOVED)
L3 20 S L2 AND PY<1999

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	ENTRY	SINCE FILE SESSION	TOTAL
FULL ESTIMATED COST		63.37	63.58

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) TOTAL	ENTRY	SINCE FILE SESSION	
CA SUBSCRIBER PRICE		-4.96	-4.96

STN INTERNATIONAL LOGOFF AT 20:45:24 ON 08 MAY 2002